PRICE DISCRIMINATION IN THE US CANCER DRUG MARKET

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Abstract

The thesis has five chapters. Chapter 1 introduces the issue. Chapter 2 discusses the concept of price discrimination, conducts a literature review, and presents a conceptual model. The literature review identified 106 articles relevant to price discrimination in the US cancer drug market. These provides the basis of a conceptual model depicting key actors and associations with price discrimination in the US cancer drug market.

Chapter 3 analyzes the evidence of price discrimination and examines demand factors suggested in Chapter 2. Using theory on price discrimination in markets with imperfect competition, price dispersion is examined in single and multi-source cancer drugs in US markets. The primary data is a large commercial claims database covering years 2010-2014. In the single source market, smaller discounts (14.7% versus 60%) and smaller levels of dispersion (5.6% versus 43%) are observed relative to the multi-source market, suggesting evidence of price discrimination. Multivariate analysis found some demand factors such as health plan and age are associated with price discrimination. Health plan type is minimally associated with price discounts. No evidence exists for type 2 price discrimination.

Chapter 4 quantifies pricing trends and assesses the impact of price discrimination in the US cancer drug market using same data from Chapter 3. For single source drugs, Average Wholesale Prices increased 76%, transaction prices increased 74%, and patient cost-sharing increased 29% from 2010-2014. The gap between the 10th and 90th percentile paid for single source drugs increased from $183 to $474. Plans with capitation and non-capitated plans experienced price increases of grew 4.3% and 5.7%, respectively. Multivariate analysis suggest a 10% increase in price dispersion is associated with a utilization increase of 1.1% in single source drugs. Each additional manufacturer is associated with a 15.5% increase in utilization.

The thesis found evidence for price discrimination in the US cancer drug market. There was evidence supporting some of the associations depicted in the conceptual model, notably the association of health plan type and price discrimination; other associations had no evidence. Results suggest a growing trend in prices and price discrimination increases access, albeit as a small effect.

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INTRODUCTION

Pharmaceuticals have been described as having different prices across markets. Some researchers have defined a market to be a country and have documented price differentials for pharmaceuticals across countries.[1] [2] Others have examined markets within countries and documented price differentials for pharmaceuticals[3] including price differentials by indication,[4] and by income.[5] Researchers have routinely discussed the levels of these price differentials, with the majority of the research focus on price differentials across countries. Danzon and Furukawa found that drug prices in the seven developed countries are on average approximately 6-33% lower than the prices paid in the US[6], other researchers have found even greater variation with a five-fold gap between the top and bottom 20th percentile.[7] Many researchers have empirically analyzed explanations behind the price differentials.[8] [9]

While researchers debate on the levels and associated factors, there is general consensus that price differentials for pharmaceuticals is attributable to the pharmaceutical company's ability to price discriminate. Price discrimination is defined as the ability of a firm to set different prices for the same product. A firm that price discriminates sets prices above the firms' marginal cost. This enables the firm to capture additional surplus from the consumer in the form of higher profits. Multiple different prices can be set

[1] Danzon, P. M., & Chao, L. W. (2000).
[2] Lichtenberg, F. R. (2010).
[3] Frank, R. G. (2001).
[4] Baslevent, C. (2005).
[5] Lichtenberg, F. R. (2010).
[6] Danzon, P. M., & Furukawa, M. F. (2003).
[7] Lichtenberg, F. R. (2010).
[8] Lichtenberg, F. R. (2010).
[9] Helble, M., & Aizawa, T. (2016).

along the demand curve to maximize profit; these multiple prices would correspond to different consumers' willingness to pay for the drug.

In a perfectly competitive market, there is no price discrimination since firms cannot act as price setters (a necessary condition for price discrimination to be discussed later). If a firm attempted to set a price above equilibrium, then in a perfectly competitive market with no barriers to entry, a new firm would enter the market and price closer to equilibrium. In the long run, with no firms able to set a price, there is only one clearing price for the market, occurring at the intersection of the aggregate market supply and demand curves.

In a classic textbook definition, price discrimination would only occur in a monopolistic market, otherwise, competing firms would enter the market if prices are above marginal costs. However, in a market with imperfect competition,[10] a firm may be in a situation where it can price discriminate by charging different prices to different consumers. Theoretical background for this suggestion is provided by Borenstein[11] and Holmes.[12] Borenstein used a spatial model of monopolistic competition and showed that competition is not a barrier to price discrimination as long as "gaps" in the market are driven by consumer brand preferences. Holmes[13] used mathematical proofs to show price discrimination could exist in situations with few suppliers. In his model, price discrimination can be explained by the ratio between the difference of two firm's own

[10] Imperfect competition is a broad term describing both monopolistic and oligopolistic competition. Both of these competitive environments have firms produce goods with some market power. It is important to note the difference between a true monopoly and monopolistic competition, as a true monopoly is one producer with no substitutes pricing at marginal revenue=marginal cost. Monopolistic competition can have multiple producers each producing a product with some monopoly power but also weak substitutes. Pricing is more flexible but often is determined by the Lerner's Markup.
[11] Borenstein, S. (1985).
[12] Holmes, T. J. (1989).
[13] Holmes, T. J. (1989).

price elasticities of demand and the cross price elasticity of demand. Both theories are similar in the sense that they both suggest price discrimination can occur in imperfect markets and is due in part to market power (products differentiable) and cross-price elasticities.

Price discrimination enables the firm to capture a greater portion of consumer surplus. The consumer surplus is transferred from the patient to the producer in the form of higher profits for the firm. Consumer surplus represents the difference between the price paid and the price the consumer is willing to pay for drug. This difference is the added benefit to the consumer of taking the drug. By shifting the consumer surplus to the producer, the drug maker is taking away the benefit of the medication for the consumer. For illustrative purposes, if a drug adds 1 year of life on average to patients with brain cancer and a patient values his/her year of life at $100,000, then a drug that costs $60,000 has a $40,000 benefit to the patient. But if the company raises the price to $100,000, then the patient loses $40,000 in benefit, and would actually be indifferent to the drug even if it adds a year of life. In this example, the $40,000 is a measure of the benefit of the drug and not an actual monetary exchange. The transfer of consumer surplus to the firm raises concerns regarding fairness, which will be discussed throughout the chapters.

For price discrimination to exist, three necessary conditions are required.[14]

1. A firm must be able to act as a price setter, such that an individual firm's demand curve is downward sloping akin to an aggregate market demand curve

2. A firm must control the sale of its product

[14] Varian, H. R. (1989).

3. A firm must be able to sort consumers by their demand (different demand elasticities for a drug)

The first condition stipulates the pharmaceutical company must be able to act as a price setter. Economists define price setters as firms that are powerful enough to set the price they charge in a market as opposed to price takers who take the price the market sets (intersection of the supply and demand curve). A key characteristic for price setters is the individual firms demand curve is downward sloping and resembles the aggregate market demand curve, as opposed to a price-taker who faces a horizontal demand curve. The price-taker's demand curve is horizontal because the market (producers and consumers) has established a market clearing price for the product. Branded drug companies are able to act as price setters because of market protections and the imperfect nature of the US drug market. For branded drugs, patent protection and market exclusivity are the main instruments that allow a pharmaceutical company to price set, since these protections prevents competitors from copying the drug and entering the market. While both instruments provide market protections, patents are issued by the U.S. Patent and Trademark Office for a fixed 20 years, while market exclusivities are granted by the Food and Drug Administration (FDA) for various time periods depending on drug application. For generic drugs, drug companies have some market power because of the imperfect competition within the drug market. A driving factor behind the imperfect competition within the drug market is barriers to entry largely due to regulatory hurdles for generics.[15]

[15] Wiske, C. P., Ogbechie, O. A., & Schulman, K. A. (2015).

The second condition required for price discrimination is that a drug company can control the sale of its pharmaceuticals. This condition is met because of legal and regulatory constraints within the pharmaceutical market. US law regulates the reselling of pharmaceuticals such that sales are often strictly limited between the wholesaler and pharmaceutical manufacturers.[16] Specific to the US, a key law limiting arbitrage of pharmaceuticals is the Prescription Drug Marketing Act (PDMA) of 1987. This law limits the resale of drugs to wholesalers, stipulates wholesale regulations, and further directs state governments to regulate wholesalers.[17] The PDMA also prevents re-importation of pharmaceuticals; therefore, preventing trans-geographic market transactions. In addition, contracts between insurer and suppliers (pharmaceutical manufacturers or wholesalers) prevent health insurers from purchasing pharmaceuticals at a negotiated price and then reselling the pharmaceuticals to other health insurers.[18] This applies to both single and multi-source drugs.

The third condition is that the drug company must be able to segment the market based on consumers' heterogeneous utilities for the drug (different demand elasticities). Consumers in the drug market can be considered either patients or payers. Patients are considered consumers since they are the people ultimately filling and consuming the drug. However, it is misleading to consider patients a typical consumer who shop and demand prescription pharmaceuticals for three reasons. First, patients are not legally able to self-prescribe; they cannot demand a drug themselves and must rely on a physician for drug demand. Second, patients rarely demand a specific drug rather they demand better

[16] Berndt, E. R., & Newhouse, J. P. (2010).
[17] Angarola, R. T., & Beach, J. E. (1996).
[18] Frank, R. G. (2001).

health and will often "consume" the products suggested by the physician. Third, and perhaps most important, insured patients in the US are rarely responsible for the full cost of the drug.[19] Instead, insured patients will typically have their prescription health plan pay the majority share of prescription costs. This relationship distorts traditional supply-and-demand competitive forces and is why health plans should be considered the primary consumer in the US cancer drug market.

Throughout the chapters, there is further discussion of the existing research on the US cancer drug market with an emphasis on how features of this market satisfy the three necessary conditions for price discrimination. The discussion of the necessary conditions is followed through with empirical analysis of the US cancer drug market using a large commercial claims database. The underpinnings of the empirical analysis often relate to the necessary conditions for price discrimination. The necessary conditions are also discussed within a context of imperfect competition in the US cancer drug market.

While there are three necessary conditions for price discrimination, economists' have also defined three distinct types of price discrimination.[20] Type I price discrimination occurs when the firm can price a product to every individual consumer's maximum reserve price. Type I price discrimination is often called perfect price discrimination since it completely transfers all consumer surplus to the producer. For this price discrimination to occur, it is necessary for the firm to know each consumers maximum reserve price, which the firm will use to set each consumers price. This price discrimination is rarely observed in the real world and exists primarily as a theoretical option.

[19] Berndt, E. R., & Newhouse, J. P. (2010).
[20] Varian, H. R. (1989).

Type II price discrimination is characterized by the firm pricing a product to consumers based on the quantity consumed by each consumer. Most often Type II price discrimination occurs when each consumer is offered a range of prices based on quantity purchased, something common in the pharmaceutical industry[21]. Type II price discrimination in pharmaceutical markets likely exists in two levels. First, drug distributors and wholesalers may be able to exact quantity discounts from the pharmaceutical company depending on quantity purchased. Second, pharmacy benefit managers or health insurers can negotiate discounts directly from pharmaceutical companies based on quantities purchased. The level of price discrimination for distributors and wholesalers should be relatively small since quantity discounting can allow for arbitrage, but could be much larger for large pharmacy benefit managers (PBMs) or health insurers that purchase large quantities of drugs and have some degree of discretion on the formularies and the tiers. In Chapter 3, empirical analysis will examine evidence for the presence of Type II price discrimination.

Finally, Type III price discrimination is when the firm offers different prices for the same product to different groups of consumers. Firms can incur Type III price discrimination by separating consumer groups by their groups' demand elasticities. For example, consider the incentives of the health insurer; an insurer, who can pass the cost onto the patient via high co-pays or coinsurance amounts, could be willing to accept higher prices since costs are partially transferred to the patient. Another example could be insurers whose plan participants are younger and therefore less likely to get cancer, and since these insurers would fill cancer drugs at low rates per beneficiary, they may be

[21] Berndt, E. R., & Newhouse, J. P. (2010).

less sensitive to the price of cancer drugs and willing to accept higher prices. Type III price discrimination is the most common type discussed in current literature on price discrimination.

In the international context, the consumer can be considered at the country level, and the country's demand elasticity for pharmaceuticals could be largely based on the country's income. Income influences demand elasticity through what economists call the "income effect", which can change the relative demand for goods as income changes. For drugs, a poor country may have higher price elasticity for cancer drugs because the Health Ministry lacks the budget to make cancer treatment a priority. Within the US, Lichtenberg suggested low and high income people had better access to lower priced drugs than middle income people.[22] Type III price discrimination will be investigated in both Chapters 3 and 4, and is found to be the predominant type of price discrimination in the US cancer drug market.

While the word "discrimination" in the term "price discrimination" often has a negative connotation, economists do not think price discrimination necessarily has negative implications. Danzon,[23] Lichtenberg,[24] and Malueg and Schwartz[25] all have argued that price discrimination in the drug market can provide benefits to society. The basis for this observation is that price discrimination increases social welfare by increasing output. Danzon[26] has been an ardent supporter of price discrimination in the drug market. She has argued against policies that either promote uniform pricing or

[22] Lichtenberg, F. R. (2010).
[23] Danzon, P. M. (1997).
[24] Lichtenberg, F. R. (2010).
[25] Malueg, D. A., & Schwartz, M. (1994).
[26] Danzon, P. M. (1997).

increase transparency and thereby limit consumer segmentation. The reason for her support of price discrimination is related to the cost structure of drugs. She notes drugs incur a significant fixed upfront cost to develop and commercialize, i.e. R&D. To encourage private sector investment, drug prices have to be high enough to allow for a net return of investment in aggregate, and under uniform pricing, this high price will limit access to drugs in certain markets.

Prices are sustained high due to the market protections in the form of patents and market exclusivity granted by the Food and Drug Administration and European Medicines Agency. These market protections allow the drug company to set prices well in excess of the marginal cost to produce the drug. In a uniform pricing environment, these high prices may be at such a level that they are unaffordable in poor countries. However, price discrimination allows drug companies to set low prices for these poor countries access the market, a suggestion not only by Danzon[27] but others[28] [29] as well including the World Health Organization.[30] With price discrimination and setting prices low enough to enter poor markets, drug companies can profit while patients in these markets can access drugs that are normally unaffordable. In general, an increase in output is considered welfare increasing. However, the benefits of price discrimination in the domestic market are less clear.

In Chapter 4, the study assesses price discrimination in the US cancer drug market. The assessment of the impact of price discrimination in the US cancer drug

[27] Danzon, P. M. (1997).
[28] Lichtenberg, F. R. (2010).
[29] Malueg, D. A., & Schwartz, M. (1994).
[30] World Health Organization. (2008). Measuring medicine prices, availability, affordability and price components.

market is based on access, fairness, and equity, with empirical analysis directly assessing the issue of access. Related, in Chapter 4, it is suggested that policymakers are less interested in welfare and more interested in access that can be correlated to social welfare.

The study focuses on the US cancer drug market for several reasons. First, cancer drugs, also known as antineoplastic, cancer, or oncologic drugs, is a large market, with 2015 US cancer drugs sales at $49 billion and expected continued growth.[31] These drugs are often high-cost with the average cost per month of branded cancer drugs estimated at $10,000.[32] Branded denotes a company's drug is protected by a patent or market exclusivity granted by either the US Patent and Trademark Office or the Food and Drug Administration (FDA) respectively. These mechanisms prevent competitors from copying the drug and entering the market, thereby limiting the supply of a drug to just one firm-creating nearly monopolistic or oligopolistic situations depending on similarities of substitutes. In addition, the high-prices are also the result of the underlying pharmaceutical market[33] that has been characterized as imperfect due to barriers to entry (expense to develop a new drug or regulatory hurdles), agency (physicians acting in both their own economic interest and the patient's interest), and asymmetric information (patients have difficulty assessing the value of a drug).[34]

The second reason for focusing on cancer drugs is related to the issue of rebates, discounts, and chargebacks. These issues are an important characteristic of the US drug

[31] IMS Institute for Healthcare Informatics. *Global Oncology Trend Report: A review of 2015 and outlook to 2020*. 2016;https://morningconsult.com/wp-content/uploads/2016/06/IMS-Institute-Global-Oncology-Report-05.31.16.pdf. (Accessed Feb. 4, 2017).
[32] Johnson, K., Blansett, L., Mawrie, R., & Di Biase, S. (2014).
[33] Bach, P. B. (2015).
[34] Rattinger, G. B., Jain, R., Ju, J., & Mullins, C. D. (2008).

market in general.[35] The way drugs are priced and sold in the market involves multiple entities notably the drug manufacturer, PBM, pharmacy, patient, and health plan. The drug manufacturer contracts with either PBMs or health plans directly to get a drug favorably on a formulary. These contracts are confidential; since the confidentiality keeps the true price hidden from competing health plans. In the contracts, drug companies often offer monetary incentives to health plans for favorable placement of the drug. These incentives include rebates, discounts, and chargebacks that kick money back to the health plan after a prescription is filled. As expected, one must question any analysis involving drug prices in the US on whether the price used reflects the true price net of rebates, discounts, and chargebacks; the true price is known as Average Selling Price (ASP). Given this concern, the cancer drug market was targeted because there is research that suggests rebates, discounts, and chargebacks are not significant in the cancer drug market due to the significant market power of drug companies.[36]

Another reason for the focus of research on cancer drugs is related to the indications. Since this study explores the role of indication on cancer drug pricing and possible price discrimination, it is important to determine a clear indication. For many drugs, there is always the potential of off-label use; off-label describes the situation where the drug is prescribed for an indication that is not marketed or approved for. Cancer drugs are rarely used off-label, therefore, the indications for the drug are truly reflective of actual indications, and this allows for better analysis on the association of price discrimination to cancer type.

[35] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).
[36] Danzon, P. M., & Taylor, E. (2010).

Lastly, the choice of high-cost cancer drugs is due to the concern of policy makers, physicians, and patients.[37] It has been reported that high costs for cancer drugs, even just the deductibles and co-pay paid by patients, is associated with lower adherence to medication[38], and adherence is critical for proper cancer care.[39] Not only does the high cost of cancer drugs act as a barrier to treatment, but it may substantially impact a patient's or his/her family's life including exhaustion of savings and personal bankruptcy.[40] In the presence of price discrimination, drugs can be priced above the normal competitive equilibrium meaning higher cost sharing which reduces adherence.

This thesis studies price discrimination in the US cancer drug market. It begins with a discussion of current literature, which provides the foundation for a conceptual model. Evidence for price discrimination is empirically analyzed. This analysis also examines the associations illustrated in the conceptual model. In the last chapter, trends in the US cancer drug market are examined, followed by an assessment of the impact of price discrimination in the US market.

Throughout this thesis, the results will be discussed with a focus on policy implications. Many results will be suggestive of the imperfect competition in the US cancer drug market. These results will add further evidence of imperfect competition in the US cancer drug market and raise concerns for market abuses (setting and increasing prices without credible explanation). The differential pricing associated with price

[37] Zafar, S. Y. (2016).
[38] Eaddy, M. T., Cook, C. L., O'Day, K., Burch, S. P., & Cantrell, C. R. (2012).
[39] Ruddy, K., Mayer, E., & Partridge, A. (2009).
[40] Meropol, N. J., Schrag, D., Smith, T. J., Mulvey, T. M., Langdon, R. M., Blum, D., ... & Schnipper, L. E. (2009).

discrimination also raises concerns for policymakers for issues of access, fairness, and equity in the US cancer drug market.

1.1 Research Methods

The overarching goal of the thesis is to better understand price discrimination in the US cancer drug market. Chapter 2 comprises a structured literature review and development of conceptual model explaining demand factors and price discrimination in the US cancer drug market. In Chapter 3, empirical analysis assesses evidence for price discrimination in the US cancer drug market and examines several of the hypothesized associations that were depicted in the conceptual model. Chapter 3 introduces the primary database for the study which is the Truven Health MarketScan® Research Database (MarketScan®) from 2010 to 2014, supplemented with Truven Health Red Book®. Chapter 4 builds upon the empirical analysis in Chapter 3 by quantifying the price trends in the US cancer drug market. The price trends analysis sets the stage for analysis of the impact of price discrimination in the US cancer drug market, and four related but distinct secondary hypotheses are examined.

Each chapter has its own primary and secondary hypotheses that are related to price discrimination in the US cancer drug market. In Chapter 2, the primary hypothesis is that price discrimination in the US cancer drug market can be explained visually by showing the associations between the five key actors (patients, payers, physicians, drug manufacturers, and government) of the US cancer drug market and price discrimination. The nature and type of associations were derived from a structured literature review targeting articles in the health and economics literature. The literature search used nine concepts to identify relevant articles: pharmaceutical price discrimination;

pharmaceutical market power; market power and price discrimination; health plan characteristics and demand for pharmaceuticals; pharmaceutical characteristics and demand; physician characteristics and demand for pharmaceuticals; patient characteristics and demand for pharmaceuticals; health policy and demand for pharmaceuticals; and pricing in the cancer drug market. A total of 1472 articles were found. These articles' abstracts were screened for relevance to some aspect of price discrimination in the US cancer drug market. After abstract screening, a total of 106 articles were deemed relevant to the study. A review of these articles motivated the associations between the five key actors of the US cancer drug market and price discrimination. These associations were depicted as a conceptual model. The model was tested empirically in subsequent chapters.

In Chapter 3, the primary hypothesis is that a market with imperfect competition will exhibit increasing levels of price dispersion as the market gets more competitive if price discrimination is present. The hypothesis was motivated by theoretical work from Borenstein[41] and Holmes[42]. Their work suggested price discrimination can occur in markets with imperfect competition, which neither have true monopolies nor do they have perfectly competition. Specifically, price discrimination can exist in imperfect markets if products (and companies) have market power, products that are differentiable, and have cross-price elasticities. The hypothesis is the price dispersion differences would exist between the two environments in presence of price discrimination exists and dispersion would be greater in the multi-source environment. This hypothesis was tested

[41] Borenstein, S. (1985). Price discrimination in free-entry markets. *The RAND Journal of Economics*, 380-397.
[42] Holmes, T. J. (1989). The effects of third-degree price discrimination in oligopoly. *The American Economic Review*, *79*(1), 244-250.

using multi-level regression analysis using five different models stratified by single source and multi-source cancer drugs for a total of ten different regression analyses. In addition, Chapter 3 has several secondary hypotheses related to the demand factors and price discrimination. The demand factors were suggested in Chapter 2's conceptual model. These hypotheses posited an association between demand factors and price dispersion. Multi-level regression analysis is conducted for the secondary hypothesis analysis. The demand factors of interest include:

1. Health plan type (e.g. high deductible health plan or health maintenance organization)
2. Health plan market share
3. Patient characteristics including age, sex, employee classification
4. Drug characteristics including overall survival and years since FDA approval

Chapter 3 also presents results from a univariate analysis comparing the demand factors listed above as well as cancer diagnoses of patients with levels of price discount and price dispersion. Similar to the regression models above, the univariate analysis was stratified by single source and multi-source cancer drugs.

Economists judge the merits of price discrimination on the change in welfare, and suggest price discrimination is beneficial if it increases welfare. They also generally posit that an increase in output is associated with more social welfare. For policy makers, the major concern is access to the drugs. Access and output is considered to be positively related. Chapter 4 uses longitudinal data to quantify pricing trends of US cancer drug market and assesses the relationship between price discrimination and access. The prices for antineoplastic agents therapeutic class drugs in a large commercial claims database

from 2010-2014 are analyzed. The trends in the US cancer drug market provides the data to assess the impact of price discrimination on utilization.

The primary hypothesis is an increase in price dispersion for a cancer drug, proxy for price discrimination, is associated with an increase in cancer drug utilization. Using the price trend and utilization data from 2010-2015, this hypothesis was tested with a linear mixed methods regression model with random effects and cluster variable around drug. This model estimated the association of changes to price dispersion with changes to cancer drug utilization while controlling for market factors including changes to price level, changes in manufacturers, and changes in discounts between transaction price and AWP. In addition to the primary hypothesis, Chapter 4 also tested four secondary hypotheses. These are:

1. The gap between the 10^{th} and 90^{th} percentile price paid for a drug will increase.
2. Health plans with capitation will see slower rates of price increases.
3. Following the transition from branded to generic drugs, cancer drugs will lower their prices, have greater dispersion, and increased use.
4. For generic cancer drugs, an increase in number of participating manufacturers will be associated with lower prices, higher dispersion, and increased utilization.

The secondary hypotheses were assessed using a variety of methods. These include univariate analysis on price trends, regression analysis, and graphical analysis. For the first hypotheses, univariate analysis and graphical analysis confirms a growing gap in prices paid. For the second hypotheses, univariate analysis suggests plans with capitation saw smaller increase as a price relative to plans with capitation. However, a t-test finds no statistical significance of this result. For the third hypothesis, there were four branded

cancer drugs that had entry of generic competition during the study sample. These four were exemestane (generic approved April 2011[43]), anastrozole (generic approved June 2010[44]), letrozole (generic approved June 2011[45]), and capecitabine (generic approved September 2013[46]). Changes in utilization, price, and price dispersion were assessed for these for drugs. For the fourth hypothesis, the regression models from the primary hypotheses were adapted to test changes in the number of unique manufacturers. This hypothesis was tested strictly in the multi-source drug sample since single source drugs had only one manufacturer by definition. This thesis uses a variety of methods to examine price discrimination in the US cancer drug market.

[43] https://www.drugs.com/availability/generic-aromasin.html [ACCESSED Feb 2, 2017]
[44] https://www.drugs.com/availability/generic-arimidex.html [ACCESSED Feb 2, 2017].
[45] https://www.drugs.com/availability/generic-femara.html [ACCESSED Feb 2, 2017].
[46] https://www.drugs.com/availability/generic-xeloda.html [ACCESSED Feb 2, 2017].

CHAPTER 2

A REVIEW AND CONCEPTUAL MODEL

KEY TAKEAWAYS

1. Current literature on price discrimination in the drug market suggests price discrimination exists across countries, incomes, and indications.
2. Structured literature review found 1472 articles, of these 106 articles were related to some aspect of price discrimination in the US cancer drug market and are discussed.
3. A conceptual model relating the five key actors of the US cancer drug market and possible associations with price discrimination is presented.

2.1 Abstract

Price differentials for drugs have been observed both internationally and within the US market. The differential pricing coupled with a drug's market power, ability to control the sale of the product, and ability to segment consumers based on their preferences suggest the potential for price discrimination. The economics and health services research literature were synthesized to create a conceptual model identifying the motivations of the five principle actors of the pharmaceutical market (health plans, patients, physicians, drug companies, and the government) and their potential influence on price discrimination. The model suggests that the four largest associations between the principle actors and price discrimination are: 1) the ability to pharmaceutical firms to segment the market and engage in price discrimination, 2) the ability of pharmaceutical firms to have market power and engage in price discrimination, 3) how health plan characteristics can contribute to market segmentation, and 4) how drug characteristics influence the level of price discrimination. This model will be tested empirically in Chapter 3.

2.2 Background

There is an extensive research literature on price discrimination in the pharmaceutical market. Most of the literature involves international price differentials. The research literature contains studies examining the price variation across countries,[47] price variation by indication,[48] and price variation associated with income.[49] The international level of price variation can be significant, Danzon and Furukawa found that drug prices seven developed countries are on average approximately 6-33% lower than the prices paid in the US[50]; other researchers have found even greater variation.[51] While some policy makers have found problems with price discrimination domestically, the World Health Organization has embraced pharmaceutical price differentiation as a way to increase access for developing nations.[52] In this paper, we will focus our attention on price discrimination domestically and more specifically focus on price discrimination in the cancer drug market.

The ability for a pharmaceutical company to charge different prices for the same product across different consumers is called "price discrimination" or "price differentiation"[53]. For firms to price discriminate, economists have identified three necessary conditions.[54]

1. A firm must be able to act as a price setter

[47] Danzon, P. M., & Chao, L. W. (2000).
[48] Baslevent, C. (2005).
[49] Lichtenberg, F. R. (2010).
[50] Danzon, P. M., & Furukawa, M. F. (2003).
[51] Lichtenberg, F. R. (2010).
[52] World Health Organization. (2008). Measuring medicine prices, availability, affordability and price components.
[53] This paper will use price discrimination.
[54] Varian, H. R. (1989). Price discrimination.

2. A firm must be able to control the sale of its product

3. A firm must be able to segment consumers by their demand (different demand elasticities for a drug).

The first condition is that the pharmaceutical company must be able to act as a price setter. Economists define price setters as firms that are powerful enough to set the price they charge in a market as opposed to price takers who take the price the market sets (intersection of the supply and demand curve). A key characteristic for price setters is the individual firms demand curve is downward sloping and resembles the aggregate market demand curve, as opposed to a price-taker who faces a horizontal demand curve. The price-taker's demand curve is horizontal because the market (producers and consumers) has established a market clearing price for the product. Branded drug companies are able to act as price setters because of market protections and the imperfect nature of the US drug market. For branded drugs, patent protection and market exclusivity are the main instruments that allow a pharmaceutical company to price set, since these protections prevents competitors from copying the drug and entering the market. For generic drugs, drug companies have some market power because of the imperfect nature of the market notably the barriers to entry due to regulatory hurdles for generics.[55]

The second condition required for price discrimination is that a drug company can control the sale of its pharmaceuticals. This condition is met because of legal and regulatory constraints within the pharmaceutical market. US law regulates the reselling of pharmaceuticals such that sales are often strictly limited between the wholesaler and

[55] Wiske, C. P., Ogbechie, O. A., & Schulman, K. A. (2015).

pharmaceutical manufacturers.[56] Specific to the US, a key law limiting arbitrage of pharmaceuticals is the Prescription Drug Marketing Act (PDMA) of 1987. This law limits the resale of drugs to wholesalers, stipulates wholesale regulations, and further directs state governments to regulate wholesalers.[57] The PDMA also prevents re-importation of pharmaceuticals; therefore, preventing trans-geographic market transactions. In addition, contracts between insurer and suppliers (pharmaceutical manufacturers or wholesalers) prevent health insurers from purchasing pharmaceuticals at a negotiated price and then reselling the pharmaceuticals to other health insurers.[58]

The third condition is that the drug company must be able to segment the market based on consumers' heterogeneous utilities for the drug (different demand elasticities). Patients may have different demand elasticities for a drug, because 1) patients may value the attributes of the drug differently; 2) the effectiveness of the drug can depend on specific patient characteristics; and 3) patients have different income levels.[59]

We also note that different demand elasticities can also apply to different public and private payers.[60] Intuitively, a payer's demand elasticity is going to be driven by the payer's budget constraint and ability to shift patient demand to other products. Danzon[61] and Frank[62] both suggest the price differential across US payers is related to the payers' demand elasticity. Within the commercially insured market, evidence of different demand elasticities is suggested by the different formularies, and comparison of spending

[56] Berndt, E. R., & Newhouse, J. P. (2010).
[57] Angarola, R. T., & Beach, J. E. (1996).
[58] Frank, R. G. (2001).
[59] Lichtenberg, F. R. (2010).
[60] Frank, R. G. (2001).
[61] Danzon, P. M. (1997).
[62] Frank, R. G. (2001).

and utilizations across plan types.[63] [64] In the public sector, it is typically constrained by budget allocations.

Economists commonly judge the merits of price discrimination by the impact on social welfare. Welfare is a measurement of the utility a particular good or service provides and typically measured in currency units.[65] In general, economists assume that if price discrimination increases output, then it increases welfare.[66] Many health economists have argued that price discrimination for pharmaceuticals allows companies to enter markets that would normally not be served in a uniform pricing environment. [67] [68] [69] Since entering new markets increases output without necessarily sacrificing output in other markets, then price discrimination of pharmaceuticals is deemed beneficial to society.

While economists may embrace price discrimination if it increases output, policy makers may take a different perspective on the topic. The policy makers' main concern is typically access, and access is not the same as welfare. Economists measure welfare as an area effect (price multiplied by quantity), while access is measured by determining if the right medications are getting to the right patients. The difference in measurement can create different judgments on the value of price discrimination when companies price discriminate across different consumer segments.

[63] Hillman, A. L., Pauly, M. V., Escarce, J. J., Ripley, K., Gaynor, M., Clouse, J., & Ross, R. (1999).
[64] Joyce, G. F., Escarce, J. J., Solomon, M. D., & Goldman, D. P. (2002).
[65] Arrow, K. (1962).
[66] Danzon, P. M. (1997).
[67] Danzon, P. M. (1997).
[68] Lichtenberg, F. R. (2010).
[69] Malueg, D. A., & Schwartz, M. (1994).

For example, consider the use of differential pricing that allows a drug to be favorably placed on different health plan formularies. In this situation, within each consumer segment (health plan) a profit-maximizing drug company may set the drug price as close to each plan's maximum reserve price. These prices may be at such a high level that access is impeded either through affordability of the patient or formulary controls. Besides access, another major consideration for policy makers is that of fairness and equity across different patient groups. For the commercially insured market of the US, most people are insured through employers and have very limited choice in health plans. For enrollees, this may mean that prices paid and ultimately premiums and cost sharing are choices out of their direct control. In the case of Type II price discrimination, in which prices reflect quantity purchased, large health plans can access lower prices; and in the case of Type III price discrimination, in which prices reflect consumer groups' demand elasticity, a capitated plan may be more aggressive in obtaining lower prices than a high-deductible plan. In either case, an enrollee's access to lower or higher drug prices is affected by the health plan's size or plan type; some enrollees will benefit, others will lose.

For both policy makers and researchers, understanding price discrimination in the US cancer drug market requires a conceptual framework. The basis of the conceptual framework will be an assessment of the five major actors[70] in the pricing and reimbursement of the US cancer drug market, and how these actors relate to the price discrimination. These five factors are drug companies, patients, physicians, public and private payers, and the government (regulatory environment).

[70] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).

It is important to note that some actors in the supply chain are missing from the model, and this is due to the focus of the conceptual model on price discrimination of cancer drugs. In this model, Pharmacy Benefit Mangers (PBMs) are assumed to be an extension of a health plans' drug demand. In addition, wholesalers are assumed to be a pass-through entity having minimal demand effect. While the five main actors have distinct motivations, they have close interactions and the nature of these relationships will be depicted in the conceptual model. For example, a health plan's (payer) cost-sharing directly influences a patient demand for drugs, but the level of cost-sharing could also be associated with a patient's choice of which drug plan to select. These five main actors form the basis for the literature review.

This paper will discuss existing literature on price discrimination in the drug market with an emphasis on factors hypothesized to be associated with price discrimination in the US cancer drug market; present a conceptual model relating these factors and price discrimination; and discuss which factors may be most important and relevant to policy makers.

2.3 Methods

The study develops a conceptual model that explains demand factors and price discrimination in the US cancer drug market. The conceptual model will be structured to show relationships between the five main actors in the US drug market and price discrimination of cancer drugs. The literature review was undertaken with a goal of identifying where researchers agreed, disagreed, and where more research was needed in

the relationship between demand factors and price discrimination in the US cancer drug market.

A structured literature review was conducted in July 2016 to identify English-language articles related to price discrimination in the US cancer drug market. The approach was first to identify articles discussing price discrimination in pharmaceuticals generally. Identifying articles discussing factors associated with market power and demand for pharmaceuticals followed this initial analysis. Lastly, articles discussing pricing in cancer drug market were identified. This approach provided the basis for identifying associations between key actors in the drug market, a drug's market power, and firm's ability to price discriminate, and tailoring these associations to the US cancer drug market.

The literature search used two electronic databases: PubMed and EconLit. These databases were chosen because they included the main articles from the fields of health sciences and economics; both of which could contribute research articles related to price discrimination in the US cancer drug market. The literature search used nine concepts to identify relevant articles: pharmaceutical price discrimination; pharmaceutical market power; market power and price discrimination; health plan characteristics and demand for pharmaceuticals; pharmaceutical characteristics and demand; physician characteristics and demand for pharmaceuticals; patient characteristics and demand for pharmaceuticals; health policy and demand for pharmaceuticals; and pricing in the cancer drug market. The first eight concepts were used to capture relevant articles to a broader drug market beyond just cancer drugs, while the ninth focused on the cancer drug market. Specific key words and the search algorithm are shown in the Appendix.

Inclusion criteria for initial selection were that the paper contained any of the possible combinations of key terms and published in a peer-reviewed journal. Both searches were conducted in July 2016. The results were initially screened to remove duplicative articles and non-English articles. The screening was followed by a review of the title and abstract to identify articles that were relevant to price discrimination in the drug market. Articles were deemed relevant if they discussed price discrimination or price dispersion in the pharmaceutical markets. These articles were further classified as to whether they pertain to price discrimination or demand factors affecting market power/price discrimination. Additionally, the ninth search concept captured articles on the pricing in the US cancer drug market since the conceptual model will be tailored to this market. Articles were then classified as US or international based on the article focus. Figure 1 is a flow chart of the literature review.

After the identification of relevant articles, these articles were read and reviewed in the preparation of developing a conceptual model explaining price discrimination in the US cancer drug market. Articles were ultimately selected based on the following subjective criteria. First, they were selected if they explicitly discussed price discrimination in the pharmaceutical market. Second, they were selected if they discussed one of the key market actors (physicians, payers, patients, drug companies, or government) and demand for pharmaceuticals either in US or international markets; and the article's results could be applied to the US drug market. Third, they focused on pricing of cancer drugs.

Examples of the types of included articles are ones discussing the role of generic entry on branded drug demand, the impact of cost sharing on drug demand, and the

impact of physician characteristics on drug demand. Examples of excluded articles are ones discussing the impact of United Kingdom's National Institute for Health and Care Excellence on specific drug availability and the role of foundation aid on antiretroviral drugs in the developing world. Neither of which are applicable to the US drug market. A third criterion was used to select relevant articles on pricing of cancer drugs, emphasizing the factors associated with cancer drug prices in the US. This criterion was motivated by the fact that the conceptual model was being designed to study the US cancer drug market, and articles on pricing of cancer drugs helped facilitate the tailoring of more general drug market articles to the US cancer drug market.

From the selected articles, the associations between the key actors of the drug market and price discrimination were identified and interpreted for the conceptual model. The results section presents overall literature review results. There is a brief section discussing articles focusing in the international context. This is followed by a discussion of articles focusing on the associations within the US drug market. And finally, the pricing of US cancer drugs is discussed, with elaborations on how pricing of US cancer drugs would be affected by the general model. Areas of agreement, disagreement, and need for further research were highlighted.

2.4 Results

The literature review provided a landscape of demand factors that affected price discrimination in the drug market. Initially, the PubMed search resulted in 1279 articles and the EconLit search resulted in 581 for a combined total of 1860 across the nine

concepts. Duplications both across the nine concepts and two databases found 283 duplicate articles. Exclusion of non-English language articles removed another 105 results.

Of the remaining 1472 articles, 106 articles were deemed relevant to price discrimination in the US cancer drug market. During the review of the abstracts, there were several reasons for exclusion of the 1366 articles. Many articles were identified in the search but were excluded during the screening process because the article focused on a specific drug's biological use. This was common in the PubMed search results. Other articles that were excluded were articles discussing "drugs" and another search term, but these articles were not discussing pharmaceuticals rather another type of drug such as illicit drugs or veterinary medications. The last common reason for exclusion was that an article discussed one of the five key actors and drug prices but did not discuss the relationship between the actor and drug demand. 106 articles were ultimately deemed relevant to price discrimination in the US cancer drug market. 74 of these 106 primarily discussed research in primarily the US market while 32 primarily discussed research primarily in the international market. 26 articles specifically addressed price discrimination and/or forms of price dispersion of drug prices, of which15 focused on international price discrimination/dispersion. 23 articles discussed cancer drug prices, with 20 focused on US cancer drug market. The other 57 articles discussed demand factors and market power/price discrimination. The majority of these were US focused (43).

The results of the literature review provide a framework for developing hypotheses for the relationships between patients, payers, physicians, and drug

characteristics on both market power and price discrimination in the US cancer drug market. These relationships are discussed in the context of international, US, and finally the cancer drug market.

2.4.1 Price Discrimination in the International Drug Market

The literature review aimed to create a conceptual model relating the key actors to price discrimination in the US cancer drug market. However, many of the articles were in the context of international drug markets: either explicitly discussing price discrimination across countries or discussing demand factors of drugs based on ex-US research. However, this literature has implications on a US cancer drug market conceptual model and will be briefly summarized.

Many articles discussed price discrimination of pharmaceuticals across different countries.[71] [72] [73] [74] [75] [76] [77] [78] [79] [80] [81] [82] [83] These articles highlight some of the reason for price discrimination and the factors associated with price differentials. All the articles agree that price differences exist and these differentials were in fact price discrimination. However, one article by Schmalenesee argues that some difference in international prices

[71] Schmalensee, R. L. (2010).
[72] Danzon, P. M., & Chao, L. W. (2000).
[73] Tetteh, E. K. (2009).
[74] Boom, A. (1991).
[75] Wagner, J. L., & McCarthy, E. (2004).
[76] Mazumdar, M., & Banerjee, D. S. (2012).
[77] Lichtenberg, F. R. (2010).
[78] Lichtenberg, F. R. (2011).
[79] World Health Organization and Health Action International. Medicine prices: a new approach to measurement 2004 [online]. Available from URL: http://www.haiweb.org/medicine prices/manual/manuals/MedicinePricesManualBrochure.pdf [Accessed 2004 Aug 14]
[80] Danzon, P. M. (1997).
[81] Hanlon, M., & Zhang, R. (2012).
[82] Darrow, J. J. (2011).
[83] Stodder, J., & Younessi, H. (2013).

could be attributable to price regimes and not solely price discrimination. [84] For these articles, relevancy for the conceptual model of price discrimination in the US cancer drug market is addressed by inquiring what factors are associated with price differentials and if these factors are applicable to the US cancer drug market.

The first major conclusion from the international literature is price discrimination of pharmaceuticals is in part due to the pharmaceutical cost structure and subsequent market protection. For branded pharmaceuticals, there is significant upfront/fixed costs in the form of research and development expense related to developing a new drug.[85] [86] In economics, this is sometimes referred to as "sunk costs." The pharmaceutical companies are given incentives to accept this large and upfront expense by the government giving them market protections, i.e. patenting and market exclusivities, for newly launched drugs. These market protections provide a drug company significant market power (and satisfy the 1st necessary condition of price discrimination) since other companies cannot create a bioequivalent competitor. For the conceptual model, this suggests a strong association between market power and price discrimination. It also suggests a link between a drug's market protection status and market power.

Other conclusions from the international literature on price discrimination relate to the factors associated with price discrimination, and how these factors relate to a conceptual model of price discrimination in the US cancer drug market. Several articles examined the price differentials.[87] [88] [89] [90] [91] [92] Many authors have noted that the level of

[84] Schmalensee, R. L. (2010).
[85] Ridley, D. B. (2005).
[86] Danzon, P. M., & Chao, L. W. (2000).
[87] Schmalensee, R. L. (2010).
[88] Tetteh, E. K. (2009).

price differential is related in part to a country's income, often measured by GDP, since income has an impact on demand.[93] [94] [95] For example, Lichtenberg found a highly significant positive correlation between per capita income and the drug price index.[96] The relationship between income and demand is an example of the "income effect".

The income effect underpins an explanatory association of price differentials across health plans in the US, when one considers a health plans premiums to be associated with income. This will be revisited when discussing price discrimination in the US market. A few articles also discussed international regulations on price differentials especially noting the relationship between branded and generic drug prices. Danzon and Chao (2000) research suggests in less regulated environments, generics have a lower price.[97] When price differentials exist for generic drugs, this suggests that the generic market is not perfectly competitive and supports the notion that the market is imperfect. In a perfectly competitive market, the drug firm faces a price equal to marginal cost, and for drugs the marginal costs tend to be very low.[98] One would not expect significant differences in marginal costs across countries for generics. The suggestion that the generic drug market is not perfectly competitive will be a crucial assumption in Paper 2 analyses, and will be further explored.

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[89] Danzon, P. M., & Chao, L. W. (2000).
[90] Wagner, J. L., & McCarthy, E. (2004).
[91] Helble, M., & Aizawa, T. (2016).
[92] Lichtenberg, F. R. (2010).
[93] Lichtenberg, F. R. (2010).
[94] Danzon, P. M., & Chao, L. W. (2000).
[95] Mazumdar, M., & Banerjee, D. S. (2012
[96] Lichtenberg, F. R. (2010).
[97] Danzon, P. M., & Chao, L. W. (2000).
[98] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).

Another area of international research assessed the impact of competition on price differentials. First, the finding that generic competition is inversely related to price, suggests that generic competition weakens market power. [99] Second, within the broad branded market, the level of competition, measured by number of drugs within the Anatomical Therapeutic Chemical classification system, was not statistically associated with price differences. Danzon and Chao reasoned that branded drug competition would only have an effect on price in therapeutically crowded classes.[100] These results highlight an important difference between generic and branded drugs. Generic drugs can have true, bioequivalent competitors from another generic drug manufacturer; however, branded drugs do not have a bioequivalent competitor, but rather can have therapeutic substitutes, and the competitive closeness of therapeutic substitutes can vary by drug and class. This is an important point to include in the conceptual model. It is necessary to examine the characteristics of the specific therapeutic class, the relevant cancer drugs, and the alternatives to drug treatment such as radiation. The level of competition among drugs within the same treatment modality and alternatives to drugs could affect market power and are depicted in the conceptual model.

The international results also included articles that examined drug demand within a country and found results applicable to the conceptual model for cancer drugs. Filippini et al[101] and Dalen[102] et al found that patient age is positively associated with the choice of brand over generic drugs. The conceptual model will link patient age to market power; however, it will be assumed to be a weak association since we assume the primary

[99] Danzon, P. M., & Chao, L. W. (2000).
[100] Danzon, P. M., & Chao, L. W. (2000).
[101] Filippini, M., Masiero, G., & Moschetti, K. (2009).
[102] Dalen, D. M., Furu, K., Locatelli, M., & Strøm, S. (2011).

consumer is the health plan in the US cancer drug market. Filippini et al also found a relationship between patients' income and demand for drugs. Similar to patient age, this is assumed to be a weak association in the model because the effect is recognized by the choice of health plan. Health plans are the entity that chooses the formulary and the entity that negotiates the price. The role of the patient is to choose the health plan.

International research has also shown that the physician age[103] [104] and physician density[105] are both associated with drug demand. Physician characteristics will be noted in the conceptual model, but similar to patient age, the association is assumed to be weak. The physician's characteristics will not be empirically tested in paper two due to lack of data on the prescriber.

The international results of the literature review are important; however, their ability to translate to the US cancer market requires caution. There are significant cultural, regulatory, and market dynamic differences between the US and other OECD countries.

2.4.2 Price Discrimination in the US Drug Market

The literature review yielded 54 articles relevant to price discrimination in the US drug market. Among the 54 articles, 11 discussed price discrimination in the US drug market while 43 discussed demand factors.

For the 11 articles that discussed price discrimination the US drug market, there were two main themes. The first theme was a recognition and discussion of price

[103] Pichetti, S., Sermet, C., Godman, B., Campbell, S. M., & Gustafsson, L. L. (2013).
[104] Dalen, D. M., Furu, K., Locatelli, M., & Strøm, S. (2011).
[105] Filippini, M., Masiero, G., & Moschetti, K. (2009).

discrimination in the US drug market. Some of these articles provide the explanation behind the price discrimination the US drug market in the framework of the three necessary conditions for price discrimination. It was generally agreed that the US drug market is imperfect thereby providing considerable market power for drug companies. There is also agreement that the US drug market is highly regulated limiting arbitrage and resale of drugs and there are significant differences across consumer segments. Specifically, Berndt and Newhouse argue that price discrimination, specifically Type III, is highly prevalent in the branded and less so in the generic drug market.[106] They point to the low price paid by VA and Medicaid, slightly higher prices paid by health maintenance organizations, even higher prices at tiered third-party payers depending on formularies, and highest prices for cash buyers is evidence of Type III price discrimination. Frank[107] and Lichtenberg[108] noted similar pattern. These results suggest a relationship between health plan and price discrimination.

Researchers also agree that market power of the company drives price discrimination. An example of market power and consumer segmentation in the US was Baslevant's article on finasteride.[109] Finasteride is the molecule in both Proscar® and Propecia®, just in slightly different quantities. Baslevant noted that while both drugs are using the same drug molecular compound, the drug Propecia® for the treatment of hair loss was priced significantly higher than Proscar® which treats enlarged prostrates. The fact that the drug is the same molecule manufactured by the same company and can be branded for two different indications and charged two different prices suggest a clear cut

[106] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).
[107] Frank, R. G. (2001).
[108] Lichtenberg, F. R. (2010).
[109] Baslevent, C. (2005).

example of price discrimination. However, finasteride is a unique example since it was branded twice, but the relationship between target indication and price is nonetheless important to note. Theoretically, assuming branded drugs are more monopolistic than freely competitive, the price premium over marginal cost is greater the less elastic the demand. [110] If elasticity were related to indication, then indication would be related to the market power and price discrimination.

Silver raised concern over Type III price discrimination for macular degeneration within the Medicare program. [111] He reported on the controversy of bevacizumab and its antibody fragment, ranibizumab. Both drugs work equally well in macular degeneration, but ranibizumab was marketed specifically for the condition and cost 40x the price of bevacizumab. Again, suggesting indication is related to pricing and price discrimination. There were a few articles that discuss price discrimination in the US primarily in a legal context.[112] [113] [114] The Robinson-Patman Act states discriminatory pricing is illegal under certain conditions notably price discrimination causes competitive injury. During the 1990s, retail pharmacies sued drug manufacturers alleging drug manufacturers offered discounts to managed care organizations but not retail pharmacies, which in essence is price discrimination since managed care organizations would ultimately pay less than retail pharmacies. This case was ultimately settled. Pertinent to the conceptual model, these articles further suggest Type III price discrimination occurs.

2.4.3 Demand Factors in the US Drug Market

[110] Danzon, P. M., & Towse, A. (2003).
[111] Silver, J. (2014).
[112] Scherer, F. M. (1997).
[113] Abood, R. R. (1985).
[114] Elzinga, K. G., & Mills, D. E. (1997).

Two conditions for price discrimination have been central in the literature on demand factors and price discrimination. First, a firm must be a price setter. This means it has to have market power to price discriminate, something that is exacerbated in the US drug market due to underlying imperfections.[115] These imperfections include barriers to entry (it is very expensive to develop a new drug and regulatory hurdles), agency (physicians acting in both their own economic interest and the patient's interest), and asymmetric information (patients have difficulty assessing the value of a drug). It is important to understand how a firm can be a price setter and whether certain factors exacerbate market power that would need to be monitored by policy makers. Second, a firm must be able to segment the market by different demand elasticities, especially for type III price discrimination in which a firm price discriminates by consumer groups. In an imperfect market, prices are set above the competitive equilibrium and the margin is associated with demand elasticities; both the Ramsey Optimal Price (ROP) Model[116] and Lerner Mark-up are based on elasticities of demand and have been used in drug markets.[117] These pricing models have been used to explain the high price of branded drugs where prices far exceed marginal costs; and these models are applicable in markets that are neither monopolies nor perfectly competitive. Therefore, the ability and level of price discrimination is best understood if one understands the demand factors that influence demand elasticities.

For drug company characteristics, the articles primarily centered on drug characteristics and their demand effects. The results can be broken into research on the

[115] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).
[116] Danzon, P. M. (1997).
[117] Danzon, P. M., & Towse, A. (2003).

relationship between branded versus generic drugs in terms of both substitutability and price, and determinants of demand. Regarding brand versus generic drugs, many authors commented on factors for substitutability. There is general agreement that the driving factor for substitutability is own price elasticities for a branded drug and cross price elasticities for generics.[118] [119] These elasticities are driven by demand determinants between branded and generic notably price levels,[120] [121] [122] amount of side effects,[123] brand-loyalty,[124] and marketing.[125]

Related to the relationship between branded and generics, some research looked at branded price in response to generic entry. While there was no consensus across studies on a uniform price effect on branded from generic entry, Kong suggested branded drugs' price may rise in face of generic entry into the therapeutic class if the branded drug is on formulary of high coverage insurers and the factor of cross-substitute between branded and generic is small.[126] Additionally, Berndt et al suggest marketing and side effect profiles could have a positive relationship to brand price when generics are available.[127] An important gap in the literature is the role of drug characteristics such as therapeutic benefit and price change over time, when not considering generic entry. The literature review found few articles discussing solely the demand for a drug based on drug characteristics, but relationships primarily researched the interaction between branded and generic drugs.

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[118] Ellison, S. F., Cockburn, I., Griliches, Z., & Hausman, J. (1997).
[119] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).
[120] Ellison, S. F., Cockburn, I., Griliches, Z., & Hausman, J. (1997).
[121] Dalen, D. M., Furu, K., Locatelli, M., & Strøm, S. (2011).
[122] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).
[123] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).
[124] Dalen, D. M., Furu, K., Locatelli, M., & Strøm, S. (2011).
[125] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).
[126] Kong, Y. (2009).
[127] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).

Another major actor is the payer; this is the health plan/health insurer. In the US, the payer may be either commercial or government. The literature on the payer and demand for drugs falls into two spheres. One body of research examines the role of insurance, type of insurance, and having no insurance on the demand for drugs. The other body of research dives into the details of coverage and examines the role of formularies and cost sharing on drug demand.

Unsurprisingly, there was consensus that insurance increased drug utilization.[128] [129] [130] [131] Research looked at both the issuance of coverage and major changes of coverage (e.g. filling Medicare Part D "donut" hole). While insurance increased utilization, some authors found it to have a more modest effect on utilization than expected.[132] [133] Other notable results include a negative price response to insurance[134], and less price elasticity to drugs targeting chronic or life-threatening conditions.[135] This last point is important to examine the relationship between type of cancer and associated mortality and drug price. The "modest" change to utilization based on insurance identifies a possible a gap in the research since these articles used older data when high cost specialty drugs were not prevalent.

Examining the role of formularies and cost sharing, researchers broadly agree on a negative relationship between restrictions (either formulary controls or increased cost

[128] Simonsen, M., Skipper, L., & Skipper, N. (2010).
[129] Lillard, L. A., Rogowski, J., & Kington, R. (1999).
[130] Einav, L., Finkelstein, A., & Schrimpf, P. (2015).
[131] Duggan, M., & Morton, F. S. (2010).
[132] Lillard, L. A., Rogowski, J., & Kington, R. (1999).
[133] Einav, L., Finkelstein, A., & Schrimpf, P. (2015).
[134] Duggan, M., & Morton, F. S. (2010).
[135] Simonsen, M., Skipper, L., & Skipper, N. (2010).

sharing) and drug utilization.[136] [137] [138] [139] There were no immediate areas of disagreement, but there were some applicable takeaways from individual studies. Sheingold and Nguyen find an inverse relationship between cost sharing and generic utilization although the association was strongest in more competitive classes.[140] Gilman et al suggests increased cost sharing have less of an impact on maintenance medications due to more inelastic demand.[141] Both results could impact either the cross price elasticities or own price elasticities of cancer drugs under different cost sharing regimes and clinical effectiveness of a drug.

The role of patient characteristics on cancer drug demand is minimal because the demand for pharmaceuticals is a derived demand. First, they are not the person ordering the drug – physicians are the person legally able to order the drug. Second, with the exception of cases where direct to consumer drug advertising works, most patients do not demand specific drugs, rather they demand improved health, and the physician acts as the agent in determining the drug. This means that the patient will be very concerned on the pharmaceutical's impact on his or her health including therapeutic benefit and side effects, and underlying characteristics can influence demand for health. Third, patients are often partially insulated from the true cost of pharmaceuticals due to the role of insurance. Finally, and perhaps the most important, the health plan not the patient determines the formulary and negotiates the price.

[136] Li, X., & Anis, A. H. (2013).
[137] Jung, K., Feldman, R., & McBean, A. M. (2014).
[138] Bernard Gibson, T., McLaughlin, C. G., & Smith, D. G. (2010).
[139] Gilman, B. H., & Kautter, J. (2008).
[140] Sheingold, S., & Nguyen, N. X. (2014).
[141] Gilman, B. H., & Kautter, J. (2008).

Recognizing these constraints, the patient still plays an important role. The patient needs to fill the prescribed drug. Patient demand for specific drugs is recognized as having some role (e.g. the direct to consumer advertising). Previously discussed literature has touched upon certain patient characteristics and drug demand. Income[142] and condition[143] could both effect patient demand.[144] These studies recognize significant variation in medication utilization and suggest part of this variation is attributable to unobserved patient characteristics. Understanding how unobserved patient characteristics affect within drug utilization is a gap in the literature that could better explain drug demand.

While the patient is the consumer of the drug, it is the physician that prescribes the drug and therefore has a strong influence on demand for the drug. The literature on the physician's role for demanding a drug follows two main themes: modifiable physician behavior and physician characteristics. Modifiable physician behavior research focuses on the impact of marketing and pharmaceutical detailing to physicians and subsequent prescribing behavior. Marketing is an important component to brand building, and Dalen et al found brand loyalty to be an important determinant in brand versus generic substitution since physicians do not have financial incentives to choose generic over branded drugs.[145] Likewise, Berndt et al found demand for antidepressants to be

[142] Lichtenberg, F. R. (2010).
[143] Gilman, B. H., & Kautter, J. (2008).
[144] Simonsen, M., Skipper, L., & Skipper, N. (2010
[145] Dalen, D. M., Furu, K., Locatelli, M., & Strøm, S. (2011).

influenced by marketing both directed to physicians and consumers.[146] More direct, Datta and Dave show physician detailing can change prescribing behavior.[147]

While the conceptual model will indicate brand loyalty as a characteristic for both the patient and physician that influences drug demand, the age of the drug will be a proxy in the empirical analysis. This proxy is based on the assumption that demand loyalty builds over time.

There is general agreement that marketing efforts and impact drug demand can influence physician prescribing behavior; however, it is also worth noting that marketing is exclusively the purview of branded drugs and not generics. Beyond the role of marketing, researchers have found relationships between for physician geographic density and physician distance to patient on the prescribing patterns where both increased density and shorter distance increases the number of office visits and subsequently drug demand.[148] [149] Age and sex of physician are also associated with prescribing patterns.[150] However, limited prescriber data in commercial claims dataset used to test the conceptual model in paper 2 limits the ability to test these hypothesized associations. While these latter characteristics are important in understanding a drug's demand elasticity, the relationship between these characteristics and market power or price discrimination is unclear.

The last actor to be discussed is the government and their role in developing the regulatory environment for cancer drugs in the US. For US policy environment, articles

[146] Berndt, E. R., Bhattacharjya, A., Mishol, D. N., Arcelus, A., & Lasky, T. (2002).
[147] Datta, A., & Dave, D. (2016).
[148] Filippini, M., Masiero, G., & Moschetti, K. (2009).
[149] Cecil, W. T., Barnes, J., Shea, T., & Coulter, S. L. (2006).
[150] Pichetti, S., Sermet, C., Godman, B., Campbell, S. M., & Gustafsson, L. L. (2013).

that discussed the US pharmaceutical market highlighted the role of the FDA and the regulatory environment in restricting market entry,[151] limiting drug resale (second condition for price discrimination), and fostering the imperfect competitive environment.[152] For US cancer drug policy, the most relevant policy is statewide implementation of oral cancer drug parity laws.[153] These laws seek to balance the financial incentives for a patient's drug choice by allowing the out of pocket expense for oral cancer drugs, typically a prescription insurance benefit, fall in the same category as physician administered drugs, typically a medical benefit and which face out-of-pocket maximums. Unfortunately, there is a dearth of research on empirical evidence for the impact of oral cancer parity laws on drug demand.

Eight of the search concepts focused on the drug market in general for while the ninth concept targeted the cancer drug market. The results of the search had one overarching theme: many cancer drugs are very expensive. Beyond this theme, research discussed two areas: trends in the cancer drug market and the value of cancer drugs. For the trends in cancer drug market, the American Society of Clinical Oncology (ASCO) published research discussing increasing costs of cancer drugs, and the impact of costs on patient access.[154] Bennett et al [155] showed that a lack of competitive pressure is a driving force behind higher cancer drug prices. Other research in trends in cancer drug market looked at international comparisons, [156] [157] drawing similar conclusions as the price

[151] Carpenter, D. P. (2004).
[152] Calfee, J. E. (2001).
[153] Printz, C. (2014).
[154] Meropol, N. J., Schrag, D., Smith, T. J., Mulvey, T. M., Langdon Jr, R. M., Blum, D., ... & Schnipper, L. E. (2009).
[155] Bennette, C. S., Richards, C., Sullivan, S. D., & Ramsey, S. D. (2016).
[156] Vogler, S., & Vitry, A. (2016).
[157] Kantarjian, H., & Rajkumar, S. V. (2015, April).

dispersion literature. Research on the trends of cancer drug prices was fairly consistent suggesting prices were increasing and not necessarily tied to improvements in a drug's effectiveness; however, authors diverged on their opinions on what to do about the trend.

Researchers proposed a variety of methods to control cost including cost-effectiveness, Medicare negotiation, and the use of evidence-based guidelines. However much of these direct methods require an assessment of the value of the cancer drug; this is the second area of research. Without going into the nuances of assessing value, most research supported a general cost effectiveness approach such that researchers can assign a dollar amount per effect. Interestingly, there is some disagreement as to whether cancer is deserving of special treatment or not, with ASCO advocating for a special cancer framework and Brock arguing there is little ethical reason for unique framework.[158] For the cancer market specific literature review, there are two main takeaways for the conceptual model. First, there is no uniform assessment of value, although clinicians generally care most about survival as an effect. Second, there is uncertainty concerning determining how the drugs are being used to treat specific cancers since drugs often target multiple indications and may be used as complements are not substitutes. This last point suggests the relationship between competition and market power is relatively weak in the cancer drug market.

2.5 Conceptual Model

The conceptual model begins with the identification of the five key actors in the US cancer drug market. The conceptual model is presented in Figure 2. In the conceptual

[158] Brock, D. W. (2010).

model figure, a subjective determination of the magnitude of the association is depicted by the relative size of the arrow.

The largest associations in terms of magnitude of impact are assumed to be the associations between market power of a drug and a drug company's ability to price discriminate; the drug company's ability to segment the market by health plan and their ability to price discriminate; the health plans' differing demand elasticities and ability of drug companies to segment the health plans' market; and drug attributes including branded and generic substitutability, indication, and market protections and these attributes contribution to market power. The first two associations reflect two of the three necessary conditions for price discrimination. The relationship between health plan and market segmentation is grounded in that the health plan is the primary consumer for cancer drugs. It is necessary for drug companies to be able to segment the market based on health plans. The health plans could have different demand elasticities based on the general plan structure (i.e. HMO, HDHP) composition of plan enrollment, and cost-sharing/formularies. The health plan's general structure and cost-sharing/formularies influences a plan's budget constraint (i.e. income effect) and ability to guide patient's drug utilization. The composition of plan enrollment is associated with the aggregate of patient characteristics in a plan since different patients are likely to choose different plans based on their medical history, income and other factors. Drug characteristics clearly influence market power based on the status of market protection i.e. patented versus generics, and side effect profile, relative effectiveness, and time on the market. As noted earlier, the time on the market is used as a proxy for brand loyalty.

The interpretation of the literature review suggests secondary associations include the associations between market power and market segmentation, patient characteristics and health plans, patient characteristics and market power, physician characteristics and market power, and government regulation and market power. Market power and market segmentation are interconnected because firms need market power to segment the market. The market power for drug firms is driven both by the market protections for branded drugs and market imperfections for both branded and generic drugs. Without market power, a firm would not be a price setter and cannot set differing prices to different market segments. Patient characteristics and health plans were associated since patient characteristics could influence drug demand and is hypothesized that patient characteristics through the aggregation at the health plan level would influence a health plans drug demand. Both physician characteristics and policy are loosely related to market power since they would affect the demand elasticity for cancer drugs.

2.6 Limitations

The study has several important limitations. The results of the literature review may have missed important and relevant articles due to the databases searched or selection of keywords. Many of the results were international or not specific to the US cancer market and their applicability to the conceptual model could be questioned. The cancer drug market could be different from other drug markets. The hypothesized relationships of the conceptual model were motivated by the literature review, but research results could have been misinterpreted. Not only could the results be misinterpreted, but much of the literature only look a specific facet of the drug market and the interaction of other parts could have significantly altered the hypothesize

relationships. Lastly, PBMs are assumed to be an extension of the health plan, but this structural assumption could be wrong. Implications of which could fundamentally alter the relationship between health plans and market power and market segmentation and ultimately price discrimination.

2.7 Conclusion

Price differentials in the US drug market coupled with a drug's market power, ability to control the sale of the product, and segment consumers based on their preferences suggest the potential for price discrimination. A structured literature review provided research and suggestive hypotheses between the five key actors in the US cancer drug market and price discrimination. The results of the literature review suggests that the four largest associations are:

1. Ability to pharmaceutical firms to segment the market
2. Ability of pharmaceutical firms to have market power
3. How health plan characteristics can contribute to market segmentation
4. How drug characteristics influence the level of price discrimination.

These associations as well as others are modeled in the conceptual model in Figure 1, and will be tested empirically in subsequent chapters. For policymakers and researchers alike, the conceptual model provides an overview of factors that are hypothesized to be associated with price discrimination in the US cancer drug market. Policies that target key associations can influence market power and price discrimination. Proactive policies

can be used to address issues on access, fairness and equity within the US cancer drug market.

2.8 APPENDIX CHAPTER 2

Figure 2.1: Literature Review Flow

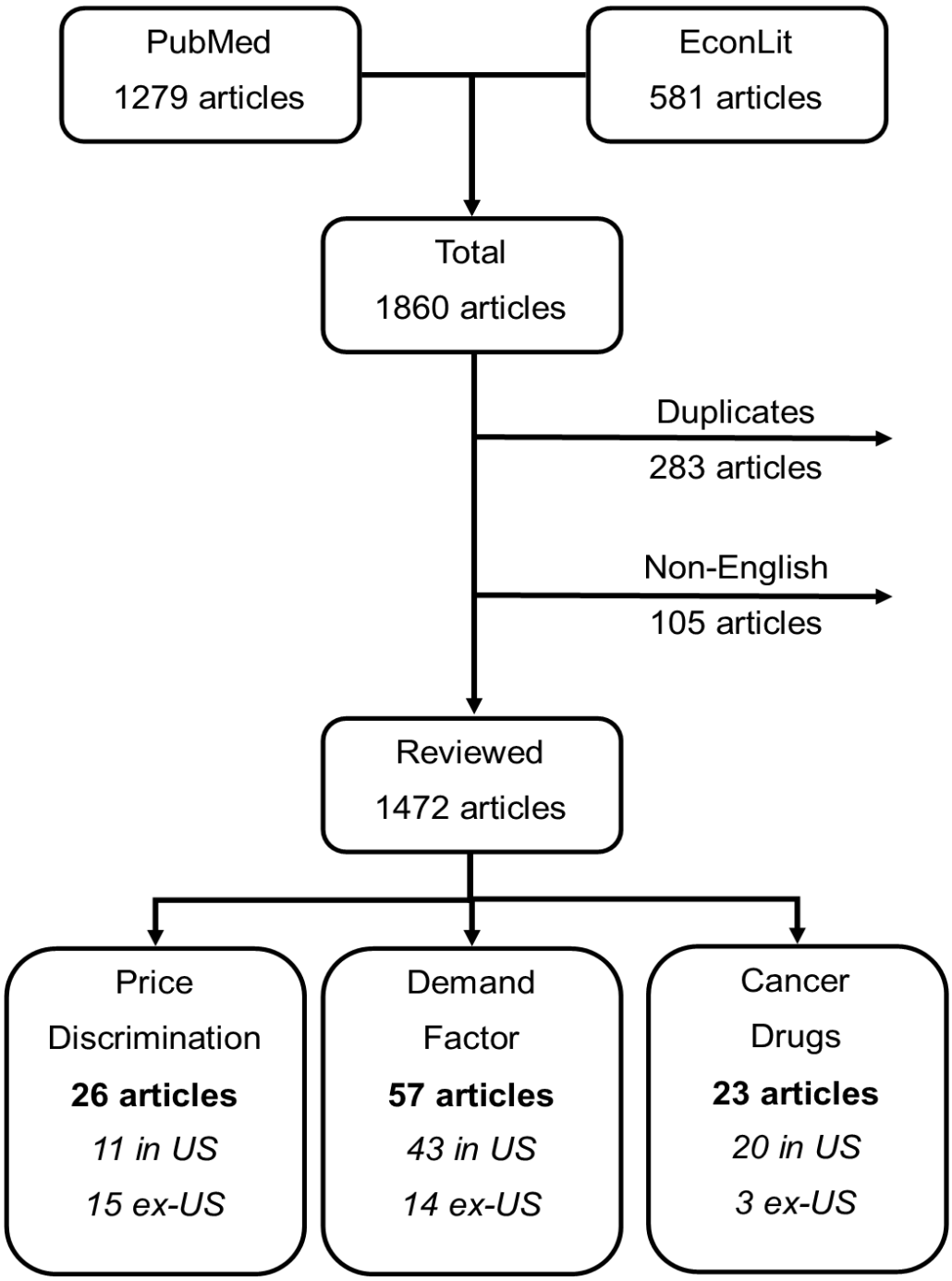
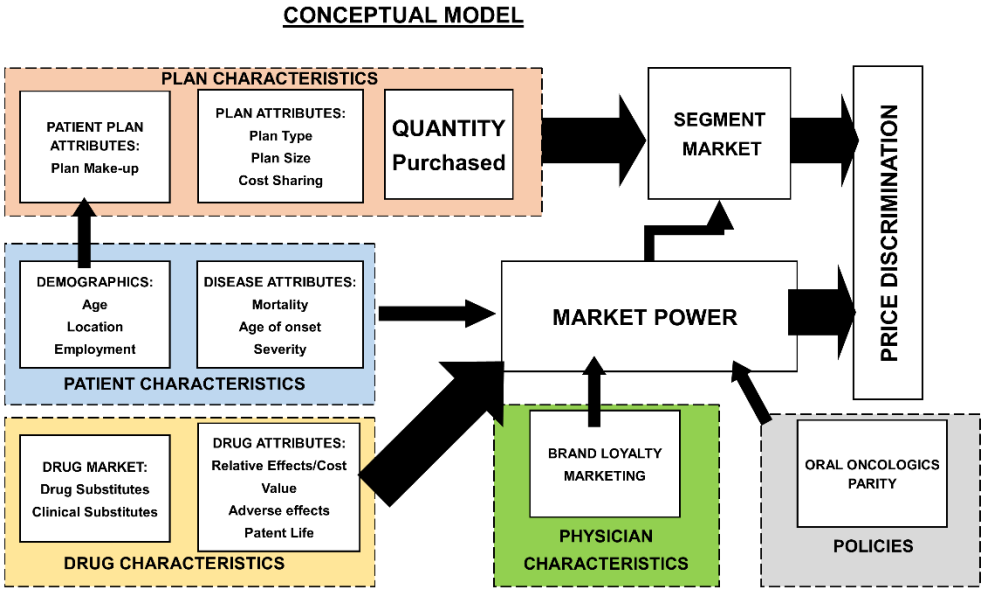


Table 2.1: Literature Review Concept

Concept	Search Terms
Price Discrimination	(drug* OR pharmaceutical*) AND ((price discrimination) OR (price differentiat*)
Market Power	(drug* OR pharmaceutical*) AND (market power)
Market Power and Price Discrimination	(market power*)) AND ((price discrimination) OR (price differentiat*))
Health Plan Characteristics and Demand	(drug* OR pharmaceutical*) AND (health plan) AND (health insur*) AND (demand)
Drug Characteristics and Demand	(drug* OR pharmaceutical*) AND ((characteristic*) OR (attributes) or (characteristic*) AND (demand)
Physician Characteristics and Demand	(drug* OR pharmaceutical*) AND ((characteristic*) OR (attributes)) AND (prescriber*) OR (doctor*) OR (physcian*)) AND (demand)
Patient Characteristics and Demand	(drug* OR pharmaceutical*) AND ((characteristic*) OR (attributes)) AND (demand) AND (patient*)
Policy and Demand	(drug* OR pharmaceutical*) AND ((characteristic*) OR (attributes)) AND (demand) AND (polic*)
Cancer Drug Pricing	(drug* OR pharmaceutical*) AND ((cancer) OR (oncologic*)) AND (pric*)

Search terms were matched to article title or abstract

Figure 2.2: Conceptual Model of Price Discrimination in US Cancer Drug Market



CHAPTER 3

ANALYSIS OF PRICE DISCRIMINATION IN THE US CANCER DRUG MARKET

KEY TAKEAWAYS

1. Within both the single source and multi-source competitive environment, there is evidence of Type 3 price discrimination, but no evidence of Type 2 price discrimination perhaps because we cannot determine the effect of PBMs.

2. Single source drugs have higher prices, lower relative and greater absolute price dispersion than multi-source drugs.

3. Theory suggests in markets with imperfect competition, price discrimination will result in greater levels of price dispersion as the environment becomes more competitive up until firms no longer hold market power. We tested this theory for cancer drugs and found that the level of price dispersion is greater for multi-source drugs than for single source branded drugs.

3.1 Abstract

This study examines the level and type of price discrimination in the US cancer drug market. Price discrimination is the ability of firms to charge different prices for the same product. Using a large commercial claims database spanning five years, the differences between transaction price paid and the average wholesale price (AWP) and variation in prices were examined. Based on theories of imperfect competition, this study's hypothesis is price dispersion will increase as level of competition increases.

The responses of single and multi-source branded and generic drugs were compared separately to test this hypothesis. The single source drug sample was comprised of 96% branded drugs and 4% single source generics. The multi-source drug sample was comprised of 95% multi-source generics and 5% branded with generic available. The single source drug sample was hypothesized to be less competitive due to additional regulatory protections associated with branded drugs.

There were fewer discounts for branded than generic drugs. The single source drugs had smaller discounts (14.7%) of transaction prices to AWP than multi-source drugs (60%). This is a manifestation of less competition. In addition, single source drugs had less price diffusion than multi-source drugs with an average coefficient of variation of 5.6% compared to 43% for multi-source drugs. This demonstrates greater price diffusion and confirms the study's primary hypothesis. However, the absolute level of price disparity was greater for single source drugs. Because they were much more expensive with a mean transaction price of $3929 compared $115, for multi-source the absolute level of price disparity was greater for single source than multi-source drugs ($220 vs. $49).

Results suggest health plan type is associated with only small variation in the level of discount with high-deductible health plans having the smallest discounts. Surprisingly, health plan size was negatively associated with the magnitude of the discount - providing no evidence for Type 2 price discrimination. The role of PBMs in the process could distort the relationship between plan size and the magnitude of the discounts. We do not know the level of discounts obtained by the PBMs. Small, but statistically significant, associations between patient characteristics, discounts and variation were observed. A drug's therapeutic benefit was not associated with price dispersion. This study suggests the US cancer drug market exhibits significant price discrimination, with greater price dispersion in the multi-source market.

3.2 Background

Price discrimination is the ability of a firm to charge different prices to different consumers for the same product. In a truly competitive market, there is no price discrimination since there is only one clearing price for the market, occurring at the intersection of the aggregate market supply and demand curves. However, in a market with imperfect competition, a firm may be able to price discriminate by charging different prices to different consumers, allowing the firm to capture a greater portion of consumer surplus and therefore transferring the consumer surplus from the patient to the producer in the form of higher profits for the firm. For this to occur, three necessary conditions are required.[159]

1. A firm must be able to act as a price setter, such that an individual firm's demand curve is downward sloping akin to an aggregate market demand curve
2. A firm must control the sale of its product
3. A firm must be able to sort consumers by their demand (different demand elasticities for a drug)

If these necessary conditions exist, then a firm may be able to price discriminate. There are three different types of price discrimination. Type I price discrimination occurs when the firm can set the price for a product to every individual consumer's maximum reserve price. It is often called perfect price discrimination since it transfers all consumer surplus to the drug company. This type of price discrimination is considered rare in the

[159] Varian, H. R. (1989).

real world.[160] Type II price discrimination occurs when the firm prices a product based on the quantity consumed by that particular consumer. Type II price discrimination occurs when the price is based on the quantity purchased. Type II price discrimination in pharmaceutical markets may exist in three levels. First, drug distributors and wholesalers may be able to exact quantity discounts from the pharmaceutical company depending on quantity purchased. Second, pharmacy benefit managers (PBM) can negotiate discounts directly from pharmaceutical companies based on quantities purchased or market size.[161] Third, health plans may be able to negotiate discounts based on the size of their plan. It is important to note that confidentiality agreements limit the observation of PBM and wholesaler discounts, and this will be a limitation discussed later in the paper. We will focus on the discounts obtained by the health plan. We believe this is the appropriate level of analysis since the person selects the health plan and not the PBM or the wholesaler.

Type III price discrimination occurs when the firm offers different prices for the same product to different groups of consumers. For cancer drugs within the commercially insured market, we are assuming that the actual consumer is the health plan and the demand of the health plan is hypothesized to be influenced by plan type and enrollee's characteristics (See Chapter 2 for conceptual model). As noted in Chapter 2, the characteristics of the individual are less important because they do not make the actual formulary or pricing decisions. For Type III to occur, the drug company needs to be able to segment the market by the consumer's demand elasticities. One possible way drug companies could engage in Type III price discrimination is to negotiate prices based on a

[160] Varian, H. R. (1989).
[161] Berndt, E. R., & Newhouse, J. P. (2010).

health plans cost sharing and formulary structure. Theoretically, the plan type (e.g. HMO), cost sharing, and formulary structure would affect a plan's drug demand elasticities. For example, the health insurer may have less price sensitivity (i.e. more inelastic price demand for drugs) if they can pass the cost onto the patient via high co-pays or coinsurance amounts since their costs are partially transferred. Alternatively, a plan with less affluent participants may be more price sensitive (more elastic price demand for drugs). Lichtenberg (2010) suggested within US prices differentials were u-shaped relative to income with poorer and richer people paying relatively less than the middle.[162] This assumption has plausibility given that Medicaid programs have limited cost sharing. Another example is with health plans comprised of younger patients and therefore less likely to get cancer may be less sensitive to the price of cancer drugs and more willing to accept higher prices. A further discussion of the three necessary conditions for price discrimination, different types of price discrimination, and associations behind Type III price discrimination is discussed in the context of the US cancer drug market in Chapter 2.

Much of the existing literature on price discrimination and pharmaceuticals focuses on drug price dispersion geographically and patient out-of-pocket expenses, and drug price discrimination internationally.[163] However, there are examples that suggest price discrimination within the US pharmaceutical market. First, it's been well documented that prices for drugs are much higher for the uninsured market compared to insured market in the range of 5-30%.[164] Given that the drugs marketed to the uninsured

[162] Lichtenberg, F. R. (2010).
[163] Danzon, P. M., & Chao, L. W. (2000).
[164] Frank, R. G. (2001).

and insured are the same and there are negligible differences exists between the production or transportation of drugs to either market, a conclusion is that the price difference is primarily the result of drug companies setting higher prices for the uninsured (substantially higher than marginal cost), in effect, price discriminating.

A source of evidence is found within the US Senate Finance Committee report *"The Price of Sovaldi and Its Impact on the U.S. Health Care System"*.[165] Senate staff examined company documents from Gilead Sciences (maker of Sovaldi), and documented internal discussion of pricing strategy. The pricing strategies clearly depicted Gilead as a price setter and discussing price levels for different payers to maximize profits. While the Senate report did not specifically mention price discrimination; the setting of different prices for the same drug implies price discrimination. A third source of evidence of price discrimination is a 1996 lawsuit brought by retail pharmacies against pharmaceutical companies allege that discounts to HMOs, hospitals, PBMs, and other managed-care organizations were in violation of the Robinson-Patman Act amendments of the Clayton Antitrust Act in part because of price discrimination.[166] This case was eventually settled with no admissions of price discrimination; however, legal analysts suggested the existence of price discrimination was not questioned, rather, it was whether the price discrimination undermined the competitive process.[167] Price discrimination is legal in the US except when it undermines the competitive process.

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[165] US Senate Committee on Finance. The price of Sovaldi and its impact on the US health care system. 2015. http://www.finance.senate.gov/imo/media/doc/1%20The%20Price%

[166] Scherer, F. M. (1997).

[167] http://www.markhamlawfirm.com/law-articles/unlawful-price-discrimination-an-obscure-antitrust-offense-by-william-markham-2013/#4 [ACCESSED JULY 2017]

Price discrimination is not immediately observable since different prices may be the result of different cost functions or market dynamics; however, one framework to study for price discrimination is to examine levels of price dispersion and at different levels of market competition. Since price discrimination is the ability to charge different prices for the same drug, researchers have used price dispersion as a proxy for a firm's ability to price discriminate in markets suspected of price discrimination such as airlines.[168] With this approach, empirical analysis of price discrimination often focused on the relationship of market power and competition on price dispersion-a proxy for a firm's ability to price discriminate.

3.2.1 Price Discrimination with Imperfect Competition

Classical economic models present price discrimination only in markets with the supplier acting as a monopolist.[169] However, several researchers have suggested price discrimination can exist in markets that are between true monopolies and perfect competition. These markets are characterized with imperfect competition. Economists consider markets to have imperfect competition if either the supplier (drug firm) or consumer (patient or health plan) has market power to set prices somewhere above the long-run competitive equilibrium.[170] Monopolistic competition where the supplier produces a product that is differentiated from other products (e.g. branded) but at the same time has some substitutability is considered imperfect competition. Same is true for oligopolistic competition where multiple suppliers produce nearly identical products but are differentiated enough and lack true substitutability, that their products are priced

[168] Borenstein, S., & Rose, N. L. (1994).
[169] Borenstein, S. (1985).
[170] Stole, L. A. (2007).

above competitive equilibrium. It is widely believed the US drug market has imperfect competition.[171] The US drug market is considered to have imperfect competition because of barriers to entry (expense to develop a new drug or regulatory hurdles), agency (physicians acting in both their own economic interest and the patient's interest), and asymmetric information (patients have difficulty assessing the value of a drug).[172]

In these markets with imperfect competition, several researchers have suggested in the presence of price discrimination, increased levels of competition leads to increase price dispersion.[173] Initially, this hypothesis seems contrary to classical theory because traditional theory necessitates market power as a requirement for price discrimination and by extension increased market power (i.e. less competition) results in increased price discrimination. However, economists have hypothesized that price discrimination in a market with imperfect competition is a unique and special case. It is considered to be on the continuum of perfect competition to monopoly.

In a market with imperfect competition, the slope is based on two parts: the consumers' price elasticity of demand and the consumers' cross-price elasticity of substitutes. For example, Trexall® (methrotrexate sodium) is a branded cancer drug used to treat a variety of cancers by inhibiting cell growth.[174] The demand for Trexall® will depend on the own-price elasticity for Trexall®. However, Trexall® also has a generic available under the molecular name "methrotrexate sodium." The generic drug is manufactured by several different manufacturers. Because of generic availability, demand for Trexall® will also depend on the cross-price elasticity of "methrotrexate

[171] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).
[172] Rattinger, G. B., Jain, R., Ju, J., & Mullins, C. D. (2008).
[173] Borenstein, S., & Rose, N. L. (1994).
[174] http://www.webmd.com/drugs/2/drug-20913/trexall-oral/details [ACCESSED: Feb 27, 2017]

sodium." The demand in the generic market could be further complicated because generic manufacturers often charge varying price for the same generic molecule.[175] This price variation can exist because of the imperfect competition in the US drug market due to barriers to entry, asymmetrical information, and problems of agency. Health plans are incentivized to get patients access to low cost generics. One approach for the health plan is to reduce copays for the use of contracted mail-order pharmacies to access lower priced "methrotrexate sodium." This is in contrast to markets with monopolistic competition where the slope of the demand curve is based solely on the consumer's price elasticity of demand since there are no other substitutes.

The ability of the health plan to steer patients to lower-priced drugs whether by steering them to use generic over brand or steering them to pharmacies with lower-priced generic manufacturer, is intuitively why price discrimination can exist in the generic market. This line of reasoning seems appropriate for the US cancer drug market, because these drugs are not absolute monopolies as defined in economics since patients have alternatives. Alternatives might include other cancer drugs that are more expensive, less effective, or have worse side effects. There are also non-drug substitutes such as using radiation or hospice care.

On the spectrum of competitiveness, branded cancer drugs should be closer to the monopolistic-end compared to multi-source cancer drugs that should be closer to the free competition-end. This assumption will be tested. The reason being is that multi-source cancer drugs have multiple manufacturers for the same drug since the formulation is no longer protected either by patent or market exclusivity. Whereas branded drugs will only

[175] https://www.bna.com/competition-generics-not-n57982077535/ [ACCESSED: Feb 27, 2017]

have competition from therapeutic substitutes but the degree of substitutability varies by drug at the therapeutic class. Some researchers have suggested the cancer drug class has few true therapeutic substitutes, rather many drugs act as complements to each other and used in combination or when other drugs do not work.[176]

For markets with imperfect competition, both Borenstein[177] and Holmes[178] independently developed theoretical models showing that increased competition is associated with more price dispersion. Borenstein used a spatial model of monopolistic competition and showed that competition is not a barrier to price discrimination as long as "gaps" in the market are driven by consumer brand preferences. In the drug market, gaps can be driven by lack of perfect substitutes in the single source market, or driven by a health plans ability to steer patients to low cost pharmacies. Holmes[179] used mathematical proofs to show price discrimination could exist in situations with few suppliers. He sets up his proofs starting with a market dominated by two firms producing similar products, yet some consumers have preference over one or the other. He suggests the price differentials associated with price discrimination is in-line with a profit-maximizing firm and can be explained by the ratio between the difference of two firm's own price elasticities of demand and the cross price elasticity of demand. In the drug markets, Holmes work is more applicable to multi-source drugs where few suppliers may exist. However, both theories are similar in the sense that they both suggest price discrimination in imperfect markets and is due in part to market power (products differentiable) and cross-price elasticities.

[176] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).
[177] Borenstein, S. (1985).
[178] Holmes, T. J. (1989).
[179] Holmes, T. J. (1989).

Both models have been applied to markets with imperfect competition outside of the health care industry and empirically analyzed.[180] In some cases, the model was confirmed, while in others it was not.[181] One empirical example was an examination of price discrimination in the U.S. airline industry using price dispersion of airline tickets.[182] They argue that different ticket prices for the same trip cannot be explained by different cost functions. They found that dispersion increases on competitive routes. These two observations taken together suggest evidence of price discrimination and higher price discrimination in more competitive but not freely competitive markets. This project will test the hypothesis that single source cancer drugs are in a less competitive environment and would show lower levels of price dispersion as compared to multi-source cancer drugs.

The study will build upon previous theoretical work and empirically analyze evidence for price discrimination in the US cancer drug market proxied by price dispersion in commercial claims data. But first, the premises of previous research must be discussed in the context of the US cancer drug market. Dispersions in prices will be assessed using claims data. While there is no direct evidence, it is assumed the cost function for drugs is relatively uniform for the same drug for different patients in different health plans. Drugs are sold directly to wholesalers who distribute the drugs nationally to all purchasers. Drugs would have identical production costs and similar means of distribution, so we would expect similar costs. Even if this assumption is

[180] Lin, H., & Wang, I. Y. (2015).
[181] Gerardi, K. S., & Shapiro, A. H. (2009).
[182] Borenstein, S., & Rose, N. L. (1994).

relaxed, production and distribution costs are small relative to prices paid for drugs[183] so dispersion in these distribution costs should have minimal effect of prices.

While it may be obvious that competition is greater in multi-source drugs and single source drugs, validating that the level of competition differs between multi-source and single source drugs is crucial for testing the primary hypothesis of this study. The level of competition will be validated three ways. First, a comparison of the discount (AWP minus transaction price) will be compared between single source and multi-source drugs. Second, a comparison of the number of unique manufacturers will be done, and the hypothesis is that single source drugs have only one unique manufacturer while multisource drugs will have multiple. Lastly, FDA approval dates will be examined to confirm that single source drugs are still under patent protection, where multisource drugs are not.

The two drug groups being compared are single source and multi-source drugs. Single source drugs are patented. Brand name cancer drugs because of their patents are assumed to be in a low competitive environment. Multi-source drugs are either generic drugs or brand drugs with generics available. Multi-source drugs are assumed to be more competitive since generics can have multiple manufacturers for the same drug. However, this does not mean that the generic market is perfectly competitive since there are regulatory barriers to enter the market, and due to these barriers, some generic drugs may have few or even one manufacturer. The aim is to compare the price dispersion for each molecule/biologic stratified by single source or multi-source.

[183] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).

Within each competitive environment (i.e. single source, multi-source), a relative level of competition will be explored by controlling the role of demand factors including health plans, patients, and drug characteristics on discounts and dispersion. These demand factors should influence market power. The relationship between demand factors and market power is discussed in Chapter 2 with an accompanying conceptual model. We would expect the demand factors to have greater magnitude of impact in the single source environment.

The main policy takeaway is a concern for access. Price discrimination is indicative of an imperfect market with firms acting as price setters.[184] We assume the firm sets the price to maximize profits, which can result in less output (less access to pharmaceuticals) compared to a truly competitive equilibrium. Under profit maximizing price discrimination, drug companies will negotiate transaction prices to maximize profit within each market segment, with the transaction prices set equal to a health plan's willingness to pay. However, the AWP price is a national price that does not vary by market conditions. The drug has the same AWP price in all markets. It is the reason why we use AWP price as a measure of competition and a standard for measuring dispersion.

Price discrimination raises concerns over access limitations for two reasons. First, a health plan's willingness to pay is not necessarily a specific patient's willingness to pay. The health plan's willingness to pay is assumed to be the average of all the enrollees in the health plans willingness to pay. However, not all enrollees will have identical willingness to pay for the same drug.

[184] Varian, H. R. (1989).

Second, many health plans in the commercially insured market are also for-profit and may restrict access especially if there is no "consumer surplus" left to share between the health plan and patient. To illustrate this point, consider a drug's reserve price for a health plan equal to the health plan's value of that drug in a patient population. The difference between the transaction price and reserve price represents the economic incentive for providing this drug to a patient population. In a price discriminatory environment, the incentive is transferred to the drug company, which implies less incentive for a health plan to provide the drug resulting potentially in a more restrictive health plan. It is possible that the PBM shares some of the profits with the drug company or the health plan. The data does not allow us to examine this possible behavior. In addition to a concern for access, there is an ethical concern with price discrimination. Because price discrimination implies some pay more and others pay less, there are potential winners and losers, and this raises questions of inequity. The U.S. population faces relatively high inequity in their access to health care,[185] but addressing inequity in a specific area of health care may still be desirable for policy makers.

3.2.2 US Cancer Drug Market

The study examines the price discrimination in the cancer drug market. The cancer drug market is of specific interest for the study for several reasons. First, cancer drugs, also known as antineoplastic, cancer, or oncologic drugs, is a large market, with

[185] Davis, K., & Ballreich, J. (2014).

2015 US cancer drugs sales at $49 billion and expected continued growth.[186] These drugs are often high-cost with the average cost per month of branded cancer drugs estimated at $10,000.[187]

Branded denotes a company's drug is protected by a patent or market exclusivity granted by either the US Patent and Trademark Office or the Food and Drug Administration (FDA) respectively. These mechanisms prevent competitors from copying the drug and entering the market, thereby limiting the supply of a drug to just one firm-creating imperfect competition with the level of competitiveness dependent on similarities of substitutes. In addition, the high-prices are also the result of the underlying pharmaceutical market[188] that has been characterized as imperfect due to barriers to entry (expense to develop a new drug or regulatory hurdles), agency (physicians acting in both their own economic interest and the patient's interest), and asymmetric information (patients have difficulty assessing the value of a drug).[189]

The high cost of cancer drugs has become a major concern for policy makers, physicians, and patients.[190] It has been reported that high costs for cancer drugs, even just the deductibles and co-pay paid by patients, is associated with lower adherence to medication[191], and adherence is critical for proper cancer care.[192] Not only does the high cost of cancer drugs act as a barrier to treatment, but it also may substantially impact a patient's or his/her family's life including exhaustion of savings and personal

[186] IMS Institute for Healthcare Informatics. *Global Oncology Trend Report: A review of 2015 and outlook to 2020*. 2016;https://morningconsult.com/wp-content/uploads/2016/06/IMS-Institute-Global-Oncology-Report-05.31.16.pdf. (Accessed Feb. 4, 2017).
[187] Johnson, K., Blansett, L., Mawrie, R., & Di Biase, S. (2014).
[188] Bach, P. B. (2015).
[189] Rattinger, G. B., Jain, R., Ju, J., & Mullins, C. D. (2008).
[190] Zafar, S. Y. (2016).
[191] Eaddy, M. T., Cook, C. L., O'Day, K., Burch, S. P., & Cantrell, C. R. (2012).
[192] Ruddy, K., Mayer, E., & Partridge, A. (2009).

bankruptcy.[193] In the presence of price discrimination, drugs can be priced above the normal competitive equilibrium meaning higher cost-sharing which reduces adherence.

3.3 Data

The study assesses evidence of price discrimination in the cancer drug market by examining levels of price dispersion in different competitive environments. The data used is the Truven Health MarketScan® Research Database (MarketScan®) from 2010 to 2014, supplemented with Truven Health Red Book®, and published literature. MarketScan® contains insurance claims for nearly 66 million Americans who have employer-sponsored health insurance. The key data files from the MarketScan® database were the drug outpatient file, the outpatient services file, and enrollee file. The Red Book® file provided information on cancer drugs. A description of the data files and variables used is in Supplementary Table 1 of the Appendix. Published literature provided information on the clinical effectiveness of the drug sample and date of initial FDA approval.

Cancer drugs and their corresponding National Drug Codes (NDCs) were identified using the antineoplastic therapeutic class indicator within the Red Book® data set. The NDCs were matched to the MarketScan® Outpatient Drug claims, and drugs were excluded if they had less than 100 observations and less than $1 million in sales over the study time period. The drugs were categorized as "single source" or "multi-source" which includes both multi-source generics and single source brands with generics based on their generic indicator in Red Book®. 96% of the observations were either

[193] Meropol, N. J., Schrag, D., Smith, T. J., Mulvey, T. M., Langdon, R. M., Blum, D., ... & Schnipper, L. E. (2009).

single source or multi-source generic. There were 62 unique products, and Table 3.1 and 3.2 provides summary statistics.

The MarketScan® Outpatient Drug claims provide detail for each prescription claim by enrollee. The claim lists the national drug code (NDC), Average Wholesale Price (AWP), number of units dispensed, payment from the insurer, payment from the enrollee, and other variables. To identify comparable drugs with same dosage and units dispensed, an AWP per unit variable was created-this serves as a reference unit. Three payment-per-unit variables were created for analysis: transaction price, payment from insurer, and patient cost-share. Both the transaction price and payment from insurer variables were derived from two variables in the MarketScan® Outpatient Drug claims. The patient cost-share was calculated the difference between the transaction price and payment from insurer. The AWP per unit and transaction price variables form the foundation of the two variables of interest: the price difference and price dispersion. Price difference was calculated as the difference between AWP per unit and transaction price for each drug claim defined in Equation 1. The price difference represents the approximate discount level; however, rebates from drug manufacturers are not represented in the transaction price suggesting the discount level has downward bias. A discussion on rebates is in the Limitations section. Price dispersion was calculated as the coefficient of variation of transaction prices within the AWP per unit transactions defined in Equation 2.

EQ 1 $$P_{diff} = \frac{AWP - P}{AWP}$$

EQ 2 $$P_{var} = \frac{P(std)}{\bar{P}}$$

The variable in Equation 1 will be used as a validation variable for the assessment of the relative level of imperfect competition in single source versus multi source drug environments. The variable in Equation 2 will be the key dependent variable that proxies for price dispersion and by extension price discrimination. The coefficient of variation was chosen as the primary measure of price dispersion because it is commonly used as a measure of variation. We also measure the gap between the 90^{th} and 10^{th} percentile of price paid for the same drug.

Other variables of interest include different consumer and drug characteristics. The consumer in the US cancer drug market can be considered on two levels: one consumer is the health plan and the other consumer is the patient. The health plan is considered the primary consumer since it is often the primary payer and leverages formulary and utilization controls to influence demand. The patient is considered a secondary consumer since they can have financial responsibility in the form of cost sharing and are ultimately responsible for filling the prescription. This analysis does not mention PBMs, as this study will assume PBMs are an extension of the health plans and their drug demand is aligned with the health plan. However, in certain circumstance this may not hold. Defining the relevant consumer is important since price discrimination can only occur if the seller can differentiate the consumers in one health plan from the consumers in another health plan.

Drug companies will set prices with each health plan or in most cases through a PBM, thereby segmenting the market by plan. Drug companies cannot price discriminate by individual patients since they do not sell directly to individual patients. However, drug companies may be able to price discriminate based on the aggregate of the patients'

characteristics within a health plan. For example, the demand mix for drugs could be different for a health plan enrolling employees in a male-dominated construction company versus a balanced male-female mix white collar company. While others have found income to be associated with US price dispersion,[194] this assertion will be controlled for in the analytic models.

The MarketScan® data categorizes health plans into seven different health plan types based on health plan structure (e.g. health maintenance organization (HMO) or high-deductible health plan (HDHP)). While the data does not provide formulary details, there are general attributes for each plan type that could influence demand for a drug. For example, HMOs and PPOs with capitation are assumed to be more price sensitive since they are incentivized to keep spending low, alternatively HDHP's or CDHP's could be better able to pass costs onto the patient via cost-sharing structures[195] and therefore be less price sensitive.

The dataset also provides a plan key for approximately 15% of the observations that links plans across data sets including enrollee data. The plan key is a 6-digit code identifying a specific health plan, and not just health plan type. The relative size of health plans measured by the relative number of enrollees is a surrogate for market share of health plan-a variable of interest for testing type II price discrimination. Due to the fact that only 15% of the sample have the 6 digit code, only models with a plan key were tested specifically for type II price discrimination; other models included the full set of observations.

[194] Lichtenberg, F. R. (2010).
[195] Waters, T. M., Chang, C. F., Cecil, W. T., Kasteridis, P., & Mirvis, D. (2011).

Besides plan types, it is important to control for patient characteristics because of the indirect demand for cancer drugs via health plan demographic make-up. The patient is identified by an enrollee variable and from this patient characteristics can be ascertained. These include age, sex, cancer diagnosis, patient's cost sharing in the form of copay and coinsurance, employee classification (e.g. hourly, union, etc.), and employee state. The cancer diagnosis was determined by linking the MarketScan® Outpatient Drug claims to MarketScan® Outpatient Services claims which lists outpatient services including the primary and secondary diagnoses in the form of ICD-9 variables. These ICD-9 diagnoses were matched to types of cancer based on ICD-9 cancer classifications.[196]

Since patients could have multiple diagnoses and multiple visits, a proportion system was implemented to identify the primary cancer diagnosis. The cancer diagnosis with the highest proportion of diagnoses is ascribed to the enrollee within a given year. Drug characteristics considered include year of FDA approval, relative therapeutic benefits defined as increases overall survival in published trial data, and number of unique manufacturers. The status of market protections, defined as either exclusivity or patented, were ascertained based on whether the drug was single source branded, in which case it was protected, or was either branded with generic options or generic. For the number of unique manufacturers, data cleaning was done to ensure name variation (e.g. "Pfizer" vs "Pfizer, Inc.") did not inflate the number of unique manufacturer.

[196] Centers for Disease Control and Prevention. (2013). International classification of diseases, ninth revision, clinical modification (ICD-9-CM). *URL: http://www.cdc.gov/nchs/about/otheract/icd9/abticd9.html [accessed 2016 Dec 16]*.

The relative therapeutic benefit was ascertained from published literature notably recent work by Howard et al.[197] and Salas-Vega et al..[198] The comparator for the therapeutic benefit was predominately standard of care. The competitive environment was compared in the single versus multi-source environment; however, the number of competitors per drug was not directly controlled. The main reason was the uncertainty in identifying true competitors since cancer drugs are often approved for multiple tumor sites and are used in combination or when others fail. Regarding the latter, consider imatinib in which one could be tempted to label dasatinib a competitor since both are approved for chronic myeloid leukemia; however, imatinib will be often administered first and dasatinib will be used primarily in a subset of imatinib cases.[199] In other words, within the single source brand, these drugs did not have true substitutes. For multi-source drugs (same molecule, different manufacturer), there are direct competitors in terms of different companies making the same generic product; however, the competition is far from perfect.

There are two important considerations when using cancer drug claims data. First, as with any pharmaceutical product, there's concern about rebates and chargebacks and whether the data set allows us to observe actual prices paid. Qualitative analysis does suggest that rebates are not prevalent or significant in the branded cancer market. A VP of a specialty pharmacy, Dr. Atheer Kaddis[200] was quoted as *"I typically don't see rebates in the oncologics, even in classes where there is competition, such as renal carcinoma, where there are seven or eight drugs. That therapy is highly individualized*

[197] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).
[198] Salas-Vega, S., Iliopoulos, O., & Mossialos, E. (2016).
[199] Kantarjian, H., Shah, N. P., Hochhaus, A., Cortes, J., Shah, S., Ayala, M., ... & Nakamae, H. (2010).
[200] http://www.managedcaremag.com/archives/2014/1/benefit-and-formulary-options-appear-specialty-pharmacy [ACCESSED Dec 12 2017]

and the drugs tend not to be substitutable. There's not a lot of opportunity for market share movement among the oncologics." Another drug pricing expert, Dr. Patricia Danzon, drew similar conclusions on rebates in cancer drugs noting the limited substitutability of many cancer drugs.[201] Both expert opinions are backed by economic theory.[202]

Ellison and Snyder's research supports the hypothesis that supplier competition is a prerequisite for countervailing power, in other words, rebates (a form of countervailing power) would not be in drug markets with limited supplier competition. The research suggests that the cancer drug market indeed has limited supplier competition.[203]

Second, outliers exist. Outliers can be the result of data entry mistakes or unique situations. It is important to minimize the impact of outliers that were due to data entry mistakes. It is also important to ensure the outliers due to unique situations do not mislead the analysis or generalizability. For example, prescription payments could be denied by insurer resulting in zero or negative payments that inflate the price dispersion. Outliers were identified as observations with negative payment values, and payments per unit that were magnitudes larger than expected (e.g. 300 units filled at a price normally fit for 30 units). These were identified through exploratory data analysis of the extreme percentiles and were excluded from final analysis. The algorithm for outliers is in the Appendix.

3.4 Methods

[201] Danzon, P. M., & Taylor, E. (2010).
[202] Ellison, S. F., & Snyder, C. M. (2010).
[203] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).

The study quantifies price discounts and dispersion in two competitive cancer drug environments. It is hypothesized that price dispersion differences would exist between the two environments if price discrimination exists and dispersion would be greater in the multi-source environment. The study began with preparation and cleaning. This included identifying cancer drugs in the Red Book® data set and linking these to MarketScan® Outpatient Drug claims, classification of enrollee cancer diagnoses, creation of payment variables, and exclusion of outliers. Standard summary statistics are presented in Table 3.2 for the cancer drugs. Univariate analysis was conducted to examine the level of price difference and price dispersion categorized by the level of market protection of a drug (single source versus multi-source generic). These results were stratified across consumer characteristics of interest including cancer diagnoses and health plan type. Results of the univariate analysis are in Table 3.3.

Multivariate analysis was conducted using two similar regression approaches, one for single source branded drugs and the other for multi-source drugs. The specific regression model is a mixed method linear model to account for random effects for each drug. Equations 3 and 4 are the full multivariate models used in the analysis. The use of drug-level random effects provides the model flexibility for potentially unobserved characteristics for each drug that could influence the pricing or price dispersion of the drug.

EQ 3 $$P_{diff_{ij}} = \beta_1[DCHAR]_i + \beta_2[PCHAR]_{ij} + \beta_3[PLCHAR]_{ij} + \beta_0 + \varepsilon_{ij}$$

EQ 4 $$P_{var_{ij}} = \beta_1[DCHAR]_i + \beta_2[PCHAR]_{ij} + \beta_3[PLCHAR]_{ij} + \beta_0 + \varepsilon_{ij}$$

DCHAR: drug characteristics including overall survival, no. manufacturers, years since approval
PCHAR: patient characteristics including age, sex, employee classification
PLCHAR: plan characteristics including plan type and plan market share

Two dependent variables were regressed: price difference and price dispersion for drug i and AWP-unit j. Independent variables include a time variable to account for the longitudinal nature of data, variables representing health plan characteristics, variables for patient characteristics, and variables for drug characteristics. The null hypothesis is that these characteristics are not associated with the level of price difference or price dispersion for either single source or multi-source drugs.

Five different regression models analyzed for the single source and multi-source drugs separately. Coefficients were compared across models. For single source, the reduced model had 626,757 observations. Since health plan market share was only available for approximately 15% of the observations, only two of the five regressions included the market share variable. For these two regressions there were 64,849 observations. For model pairs that had the same number of observations, a log-likelihood ratio test was performed. The null hypothesis of this test is that the simpler (fewer explanatory variables) was the true model. Results of these models are in Table 3.4 (dependent variable: discount) and Table 3.5 (dependent variable: coefficient of variation). Variables were deemed statistically significant at the $p \leq .05$ level.

Evidence for price discrimination was assessed by examining levels of dispersion between the two competitive environments, and by comparing coefficients across model results for direction, magnitude, and significance. Qualitatively, there's reason to believe

the price discrimination exists since branded cancer drugs satisfied three prerequisites, but we need to reject the null hypothesis based on the empirical testing of the models.

The key test for price discrimination is that the level of price dispersion is higher in multi-source drugs compared to single source drugs. Within each competitive environment, another test for price discrimination is the examination of the coefficients for drug characteristics such as relative therapeutic benefit and number of manufacturers since these characteristics would have the most influence on a competitive environment. If health plans and indirectly patients negotiate with drug manufacturers when setting a price, then one would expect the drug characteristics especially relative therapeutic benefit to have significant magnitude and significance. The reason being is that an individual drugs therapeutic benefit will be most likely related to market power and a manufacturer would not be able price discriminate if it did not have market power. Patients and health plans will be more sensitive to drugs that have greater therapeutic benefit.

3.5 Results

A total of 62 distinct cancer drugs, entailing 304 NDCs and 4.7 million prescription fills for 602 thousand patients from the years 2010-2014 were analyzed. Of 62 drugs, 46 were single source brand drugs and 19 were multi source, with 3 overlapping due to expiration of exclusivity.

The average difference between AWP and total payment for single source brand drugs is 14%, and 60% for multi-source drugs. In drug pricing, and AWP is the

benchmark price and manufacturers make the greatest profit when the price gets close to the AWP; in a noncompetitive environment you would expect the manufacturer to set prices close to the AWP. In a more competitive environment, the gap between AWP and transaction price should be significantly larger.

The coefficient of dispersion for single source brand drugs across plans is 5.6%, and 43% for multi-source drugs. The higher variation suggests rejection of the null hypothesis that price discrimination does not exist and level of dispersion is the same across competitive environments.

It is important to look at both the relative differences in dispersion and the dollar amount of the dispersion. While 43% is higher than the 5.6%, multi-source drugs which has a mean reimbursement of $115 and so the 43% indicates standard deviation of $49. However because the mean reimbursement for single source oncologic drugs is $3929, the dollar value for the dispersion is actually greater ($220). In other words, while the relative level of dispersion is higher in multi-source, the dollar amount of dispersion is lower than single source. For policy makers, the dollar amount of dispersion may be more important than the relative distribution. For single source drug, the average gap between prices paid at 10^{th} percentile drug reimbursement 90^{th} percentile is $257. For some drugs, gap is larger, i.e. the gap for imatinib is $530. The absolute difference may be more important to policy makers.

Univariate analysis was conducted for plan, patient, and drug characteristics. Refer to Table 3.3 for results. The differences are relatively small across the health plans especially for single source branded drugs. The most common health plan type in the sample was a Preferred Provider Organization (PPO). For single source drugs,

Comprehensive Health Plans had the largest discount to AWP for single source branded at 15.3%, while High Deductible Health Plans had the smallest discount at 13.4%. For multi-source drugs, Point of Service plans with capitation (POS) had the smallest discount to AWP for multi-source drugs at 50.9% while Point-of-Service plans without capitation had the largest discount at 61.1%.

Market share was related to price dispersion in a very small amount. We compared the difference in price discounts for plans with more and less than 5% market share. In the univariate analysis, plans with 1-5% market share had the smallest discount to AWP for single source branded, while plans with greater than 5% market share had the smallest discount to AWP for multi-source drugs. This is counter intuitive especially in light of an hypothesis or 2nd degree price discrimination, which suggests larger plans would have access to lower prices. However, it may be the case that the larger plans have more restrictive formularies and drug companies counter the restriction with higher prices. Alternatively, PBMs may negotiate prices for several plans and the market size indicator is flawed. However, the analysis does not show the health plans with the larger market share consistently getting the highest discounts.

We examined the differences by type of cancer and demographic characteristics. Breast cancer was the most common cancer diagnoses. Other common types include non-melanoma skin cancer and bone cancer. Few patterns were noticed in the price difference and dispersion across cancer types, although breast cancer had larger discounts than most cancers. For patient characteristics, no noticeable differences in discounts or dispersion were observed for employment type, and for sex, males had a slightly larger discount. Interestingly, the middle age group (26-45 year olds) had the smallest discount

for single source branded drugs, and the youngest group (<26 year olds) had the smallest discount for multi-source drugs. These results suggest within a competitive environment either single or multi-source, the age of patients within each drug may be correlated with cancer types. This is hypothesized to effect demand and this affects a drug's competitive leverage.

For drug characteristics, no difference was observed for relative therapeutic benefit for branded drugs. This is surprising because it would be assumed that patient's would be responsive to the level of therapeutic benefit. One interpretation of this surprising result is that prices of branded drugs are set using existing drug prices plus additional margin,[204][205] and not on a drug's relative effectiveness. In order to compare the effect of competition, a binary variable indicating 7 or fewer manufacturers vs. 8 or more was created. Drugs with fewer distinct manufacturers (less competition) had smaller discounts and less price dispersion compared to drugs with more distinct manufacturers.

While the univariate results provide an overall landscape of price dispersion in the US cancer market, the multivariate regression results take into consideration the competing factors of demand and price dispersion. Two multilevel linear regression models were performed across five subsets of data with random effects at the drug product level. Results from models using the pay difference dependent variable are reported in Table 3.4, and results from models using the pay dispersion dependent variable are reported in Table 3.5. For interpretation sake, the negative sign for pay difference was flipped i.e. -10% becomes 10%. Since market share was only ascertained for a subgroup of health plans, model testing was conducted between models with market

[204] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).
[205] Salas-Vega S., Iliopoulos, O., & Mossialos, E. (2016).

share and between models without market share. The log likelihood ratio test suggest models with the full complement of independent variables provided better explanatory power as compared to simpler models with fewer variables.

Across models that were not restricted to observations with market share (Models 1-3), statistical significance was observed for many variables. This is not surprising given the large sample sizes. There are a few general trends to note. The positive sign and significance of the year variable suggests an increasing trend of greater discounts and price dispersion across all models for both single and multi-source drugs. The coefficients for many health plan types were statistically significant. In the single source drugs, POS plans pays slightly higher than other health plans; however, the magnitude of difference between plan types is generally minimal (1.6 percentage point difference between highest and lost paid plan type in the single source drugs). In multi-source drugs, HDHP plans pay the least. POS plans are also associated with greater price dispersion for multi-source drugs, perhaps suggesting a wider range of benefits across plans categorized as POS.

In the presence of 3rd degree price discrimination in which drug companies price discriminate across plan types, one would expect differences in the level of discounts, which is confirmed albeit small. Additionally, the level of discounts for plan types should vary more in the competitive multi-source environment compared to the single source environment, again confirmed as seen in Table 3.3.

Interestingly, the log of market share for single source drugs is a negative statistically significant coefficient, which is interpreted as for every 1% increase in market share, plans pay on average .2% higher relative to other plans. This is

counterintuitive and this will be discussed later in this chapter. Age, measured in years, has a statistically significant impact, but it is practically minimal. Females are associated with slightly lower discounts, again with minimal impact. Being an hourly employee is associated with an incrementally larger discount. Perhaps one of the most interesting findings is a drug's relative therapeutic benefit is not associated with the size of a discount for single source drugs.

3.6 Discussion

The US cancer drug market is a significant market with nearly $49 billion in sales in 2015[206] and generally dominated by single source branded drugs. Given the market power of these drugs, limited ability to arbitrage by wholesalers and intermediaries, and the general fragmentation of the US health care market, one would expect some level of price dispersion. The study shows that price dispersion exists both for single source or multi-source drugs with the magnitude of dispersion greater for multi-source drugs but the dollar amount greater for the single source. This confirms the hypothesis that in imperfect markets, in the presence of price discrimination, dispersion would be greater as the competitive environment increases.

One of the principal aims of this study was to assess evidence for price discrimination. Circumstantial evidence suggests price discrimination should exist for the single source brand market since the single source branded drugs satisfy the prerequisites of price discrimination. These branded drug companies are price setters;

[206] http://www.imshealth.com/en/about-us/news/ims-health-study-global-market-for-cancer-treatments-grows-to-107-billion-in-2015-fueled-by-record-level-of-innovation [ACCESSED: Jan 18 2017]

there is limited arbitrage in the market due to regulations; and companies can differentiate consumers who have different utilities. The study established that dispersion exists and the level of price dispersion is greater in the more competitive environment - suggesting price discrimination.[207] [208]

While this study was unable to fully extricate the role of bargaining and PBMs versus price discrimination in dispersion of prices, there are two potential findings that could support price discrimination in the US cancer market. First, the dispersion in prices for single source branded drugs should be lower than the dispersion in prices for multi-source drugs if the health plans key bargaining leverage is multiple competing drugs and cross-price elasticity to competitors. For the most part, single source branded drugs would compete with other drugs within their targeted therapeutic area. Therefore, a health plan's ability to bargain is limited to essentially the placement of the single source branded drug on a specific tier or the use of utilization controls and therapeutic equivalents including non-drug treatments such as radiation chemotherapy. However, the countervailing power to bargain for lower prices is limited by lack of supply competition in single source branded drugs. More practically, for the drug company, placement on a formulary tier is important as it determines a patient's co-pay and coinsurance, but the impact could be mitigated with the use of coupons and patient assistance programs. Specifically, coupons and patient assistance programs would offset a patient's co-pay only for branded drugs; these mechanisms give branded drugs even greater market power.

[207] Borenstein, S. (1985).
[208] Holmes, T.J. (1989).

Secondary analysis of the study showed that patients' co-pays and coinsurance for branded drugs were relatively low representing just 3% of total payment for each drug, possibly due to the impact of coupons or out-of-pocket maximums being reached. In essence, there is little reason for a single source branded drug to accept lower negotiated prices from a payer unless there are therapeutic equivalents. If there is little reason to accept lower prices, then the dispersion observed could be due to price discrimination by the drug company. Price discrimination may enable drug companies to be placed more favorably across formularies thereby generating higher utilization and profits, then a uniform pricing environment.

The second possible evidence suggestive of price discrimination is the lack of magnitude and significance of the coefficient for the relative therapeutic benefit for single source branded drugs. Under the hypothesis that the health plan negotiates with drug companies as equals, one would expect the health plan to negotiate bigger discounts for drugs with less therapeutic benefit relative to drugs with more therapeutic benefit. However, this was not observed, and reinforces previous literature that suggests pricing and effectiveness of the drug are not linked.[209]

3.7 Limitations

The study has several limitations. First, as discussed in the data section, there are two important considerations when using cancer drug claims data: rebates/coupons/chargebacks, and outliers. One of the motivations for examining cancer drugs is the general consensus from experts that rebates/coupons/chargebacks are not widely prevalent in this therapeutic class. For outliers, the database required significant

[209] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).

data cleaning, and summary statistics and histograms were widely used throughout the process to identify areas of concern. The data cleaning was spent to reduce for outliers due to inaccuracies of the data set, but a limitation is that the data cleaning may have eliminated some for naturally occurring outliers that are important for policymakers to consider given the skewness of healthcare spending.

The last notable limitation is the limited generalizability of the US cancer drug market to other markets such as other therapeutic classes or even other countries. Other entities, notably the National Institute of Clinical Excellence in England has recognized the uniqueness of the cancer drug market and proscribes cancer drug specific regulations.

3.8 Policy Takeaways

In a truly competitive efficient market, price dispersion does not exist since any deviance of prices would entice new competitors and arbitrage. Price dispersion does exist in both the single and multi-source cancer drug market, reinforcing the notion that the market is imperfect and price discrimination exists. Researchers have suggested price discrimination in pharmaceuticals improves societal welfare by facilitating pharmaceuticals to be priced at levels to access markets that would otherwise not be served under a uniform price system.[210] However, for policy makers a driving concern is patient access. This study has shown lower discounts, higher prices, and less price dispersion in the US single source cancer drug market relative to multi-source drugs. All three attributes will limit access to these drugs by limiting affordability. While price

[210] Danzon, P. (1997).

discrimination enables companies to access different market segments (i.e. health plan), within each market segment prices could be set high thereby limiting access through affordability or formulary controls.

Policy makers can address the imperfect aspects of the US pharmaceutical market using a variety of policy levers. However, policymakers must recognize that the market is imperfect and accept that imperfect markets have consequences.

First, economic theory suggests monopolist and oligopolists will rationally price higher than a competitive equilibrium resulting in less quantity supplied; one might consider the high price and limited uptake of the novel hepatitis C drugs as an example. Because of high prices, less than 15% of people with hepatitis C are actually receiving the drug. Second, price dispersion ultimately means some patients either through premiums or co-pays will pay more than other patients. This should be a significant concern for policymakers especially within the US where significant inequities exist.[211] The difference between the 10^{th} and 90^{th} price paid in single source drugs is $300, but for some high priced drugs that gap increases to above $500. If the patient is paying a significant percentage of the cost of the drug then price discrimination can have a large impact on the out-of-pocket spending. Lastly, for policymakers price discrimination represents a transfer of consumer surplus to pharmaceutical companies in terms of higher profits.

[211] Davis, K., & Ballreich, J. (2014).

3.9 Conclusion

The US cancer drug market satisfies all three necessary conditions for price discrimination. This study suggests price discrimination does exist based on the existence of less price dispersion for single source drugs and increased price dispersion for multi-source drugs. For single source drugs, the gap between the 10^{th} and 90^{th} price paid may be small relative to total prices, but still significant in the absolute. Some hypothesized demand factors were associated with relative levels of dispersion as suggested in Chapter 2's conceptual model.

3.10 APPENDIX CHAPTER 3

Table 3.1: Summary of Cancer Drugs in the US Market 2010-2014

Drug	Molecule	Mean AWP ($)	Mean Transaction Price	N
AFINITOR	Everolimus	$11,214	$9,585	17,874
ANASTROZOLE	Anastrozole	$544	$184	158,997
ARIMIDEX	Anastrozole	$638	$436	90,908
AROMASIN	Exemestane	$639	$519	46,969
AVASTIN	Bevacizumab	$6,530	$5,522	534
BICALUTAMIDE	Bicalutamide	$717	$178	18,204
BOSULIF	Bosutinib	$10,015	$8,347	479
CAPECITABINE	Capecitabine	$2,382	$1,900	13,309
CAPRELSA	Vandetanib	$11,951	$10,241	453
COMETRIQ	Cabozantinib Malate	$12,806	$10,981	188
CYCLOPHOSPHAMIDE	Cyclophosphamide	$468	$338	20,291
ERIVEDGE	Vismodegib	$10,204	$8,713	807
ETOPOSIDE	Etoposide	$1,390	$1,071	2,317
EXEMESTANE	Exemestane	$673	$429	112,980
FARESTON	Toremifene Citrate	$1,227	$1,047	4,618
FASLODEX	Fulvestrant	$675	$524	240
FEMARA	Letrozole	$7,072	$6,133	166,049
GILOTRIF	Afatinib Dimaleate	$8,453	$7,223	640
GLEEVEC	Imatinib Mesylate	$6,584	$5,597	84,948
HERCEPTIN	Trastuzumab	$4,953	$4,246	676
ICLUSIG	Ponatinib Hydrochloride	$12,366	$10,583	440
IMBRUVICA	Ibrutinib	$10,729	$9,134	2,345
INLYTA	Axitinib	$10,512	$8,997	2,583
LETROZOLE	Letrozole	$654	$295	119,963
LEUPROLIDE ACETATE	Leuprolide Acetate	$407	$236	56,157
LUPANETA PACK	Leuprolide Acetate;Norethindrone Ace	$2,105	$1,779	791
LUPRON DEPOT	Leuprolide Acetate	$2,599	$2,148	65,014
MEGACE ES	Megestrol Acetate	$1,671	$1,405	9,353
MEGESTROL ACETATE	Megestrol Acetate	$749	$638	60,755
MEKINIST	Trametinib Dimethyl Sulfoxide	$80	$43	1,083
MERCAPTOPURINE	Mercaptopurine	$10,341	$8,741	313,733
METHOTREXATE	Methotrexate Sodium	$244	$105	581,342
METHOTREXATE SODIUM	Methotrexate Sodium	$100	$30	1,697,232
NEXAVAR	Sorafenib Tosylate	$74	$30	10,290
NILANDRON	Nilutamide	$8,781	$7,516	517
POMALYST	Pomalidomide	$12,566	$10,688	879
RITUXAN	Rituximab	$13,482	$11,468	1,913
SPRYCEL	Dasatinib	$9,478	$8,047	21,771
STIVARGA	Regorafenib	$11,786	$10,195	2,655
SUTENT	Sunitinib Malate	$8,841	$7,533	15,379
TAFINLAR	Dabrafenib Mesylate	$8,431	$7,170	1,175
TAMOXIFEN CITRATE	Tamoxifen Citrate	$122	$29	655,964
TARCEVA	Erlotinib Hydrochloride	$6,092	$5,206	27,836
TARGRETIN	Bexarotene	$8,808	$7,628	1,342
TASIGNA	Nilotinib Hydrochloride	$9,005	$7,688	14,502
TEMODAR	Temozolomide	$2,865	$2,444	49,043
TEMOZOLOMIDE	Temozolomide	$2,783	$2,123	15,066
TREXALL	Methotrexate Sodium	$174	$146	7,866
TYKERB	Lapatinib Ditosylate	$4,522	$3,864	12,764
VALCHLOR	Mechlorethamine Hydrochloride	$4,979	$4,434	226
VELCADE	Bortezomib	$6,433	$5,453	133
VOTRIENT	Pazopanib Hydrochloride	$7,199	$6,141	9,768
XALKORI	Crizotinib	$13,236	$11,387	2,880
XELODA	Capecitabine	$1,715	$1,465	95,444
XTANDI	Enzalutamide	$9,298	$7,904	2,601
ZELBORAF	Vemurafenib	$11,480	$9,980	2,908
ZOLINZA	Vorinostat	$9,196	$7,774	528
ZYKADIA	Ceritinib	$15,674	$13,625	141
ZYTIGA	Abiraterone Acetate	$7,295	$ 6,229	8,142

Table 3.2: Price Difference and Price Dispersion for Cancer drugs

Drug	Frequency	Single Source	Brand with Generic	Multi Source Generic	Single Source Generic	Number of Manufacturers	Pay Dispersion	Pay Difference
AFINITOR	17,874	17,874	0	0	0	3	.038	-.144
ANASTROZOLE	158,997	0	0	155,771	3,226	20	.641	-.706
ARIMIDEX	90,908	73,539	17,369	0	0	1	.086	-.159
AROMASIN	46,969	39,587	7,382	0	0	2	.324	-.162
AVASTIN	534	534	0	0	0	1	.041	-.155
BICALUTAMIDE	18,204	0	0	18,204	0	12	.574	-.747
BOSULIF	479	479	0	0	0	1	.049	-.153
CAPECITABINE	13,309	0	0	13,309	0	2	.147	-.213
CAPRELSA	453	453	0	0	0	1	.019	-.139
COMETRIQ	188	188	0	0	0	1	.026	-.143
CYCLOPHOSPHAMIDE	20,291	0	0	19,819	472	2	.173	-.240
ERIVEDGE	807	807	0	0	0	1	.023	-.147
ETOPOSIDE	2,317	0	0	2,317	0	1	.130	-.218
EXEMESTANE	112,980	0	0	112,980	0	3	.275	-.364
FARESTON	4,618	4,618	0	0	0	2	.108	-.143
FASLODEX	240	240	0	0	0	1	.023	-.145
FEMARA	166,049	154,433	11,616	0	0	3	.069	-.153
GILOTRIF	640	640	0	0	0	1	.058	-.135
GLEEVEC	84,948	84,948	0	0	0	3	.055	-.146
HERCEPTIN	676	676	0	0	0	1	.026	-.151
ICLUSIG	440	440	0	0	0	1	.034	-.145
IMBRUVICA	2,345	2,345	0	0	0	1	.051	-.149
INLYTA	2,583	2,583	0	0	0	1	.087	-.142
LETROZOLE	119,963	0	0	105,999	13,964	11	.606	-.551
LEUPROLIDE ACE	56,157	0	0	51,756	4,401	4	.417	-.399
LUPANETA PACK	791	791	0	0	0	1	.069	-.150
LUPRON DEPOT	65,014	56,611	0	0	8,403	2	.058	-.149
MEGACE ES	9,353	9,353	0	0	0	1	.051	-.147
MEGESTROL ACE	60,755	0	0	60,755	0	4	.370	-.576
MEKINIST	1,083	1,083	0	0	0	1	.034	-.155
MERCAPTOPURINE	313,733	0	0	313,733	0	5	.426	-.567
METHOTREXATE	581,342	0	0	581,342	0	8	.433	-.610
METHOTREXATE NA	1,697,232	0	0	1,697,232	0	8	.422	-.619
NEXAVAR	10,290	10,290	0	0	0	2	.049	-.143
NILANDRON	517	517	0	0	0	1	.050	-.148
POMALYST	879	879	0	0	0	1	.025	-.151
RITUXAN	1,913	1,913	0	0	0	1	.039	-.149
SPRYCEL	21,771	21,771	0	0	0	1	.056	-.151
STIVARGA	2,655	2,655	0	0	0	2	.063	-.135
SUTENT	15,379	8,080	0	0	7,299	2	.040	-.145
TAFINLAR	1,175	1,175	0	0	0	1	.029	-.152
TAMOXIFEN CITRATE	655,964	0	0	655,964	0	6	.498	-.712
TARCEVA	27,836	27,836	0	0	0	1	.045	-.145
TARGRETIN	1,342	1,342	0	0	0	2	.076	-.147
TASIGNA	14,502	14,502	0	0	0	3	.041	-.147
TEMODAR	49,043	48,910	133	0	0	2	.057	-.144
TEMOZOLOMIDE	15,066	0	0	9,490	5,576	2	.171	-.240
TREXALL	7,866	7,866	0	0	0	3	.071	-.150
TYKERB	12,764	12,764	0	0	0	1	.045	-.144
VALCHLOR	226	226	0	0	0	1	.061	-.111
VELCADE	133	108	0	0	25	1	.022	-.159
VOTRIENT	9,768	9,768	0	0	0	1	.040	-.147
XALKORI	2,880	2,880	0	0	0	1	.035	-.143
XELODA	95,444	90,884	2,051	0	2,509	2	.058	-.146
XTANDI	2,601	2,601	0	0	0	1	.038	-.150
ZELBORAF	2,908	2,908	0	0	0	1	.091	-.131
ZOLINZA	528	528	0	0	0	1	.079	-.153
ZYKADIA	141	141	0	0	0	1	.047	-.130
ZYTIGA	8,142	8,142	0	0	0	1	.054	-.146

Table 3.3: Price Variation and Differences across Factors

Health Plan Characteristics	Multi Source		Single Source		Cancers	Multi Source		Single Source		Employee Characteristics	Multi Source		Single Source	
	Variation	Difference	Variation	Difference		Variation	Difference	Variation	Difference		Variation	Difference	Variation	Difference
Comp 101,026 20,070	.427	-.611	.056	-.156	BONE 213,443 66,092	.424	-.583	.055	-.147	Salary 736,679 115,815	.439	-.609	.056	-.154
EPO 63,343 10,123	.425	-.594	.056	-.144	BRAIN 23,594 69,024	.270	-.372	.056	-.148	Hourly 690,500 106,012	.436	-608	.056	-.153
HMO 514,270 84,508	.429	-.608	.056	-.141	BREAST 1,026,194 185,286	.440	-.581	.060	-.152	Other 1,427,179 221,827	.437	-.609	.056	-.153
POS 263,597 44,903	.435	-.611	.056	-.153	COLON 23,892 51,651	.288	-.417	.055	-.144	Male 951,786 205,895	.429	-.606	.055	-.146
PPO 2,364,970 372,691	.430	-.595	.055	-.146	HEAD 24,193 53,273	.376	-.527	.048	-.145	Female 3,034,750 422,085	.429	-.595	.057	-.148
POS w/cap 27,495 4,003	.423	-.509	.057	-.149	LEUKEMIA 32,427 99,942	.427	-.588	.053	-.147	**Age**				
CDHP 241,870 33,863	.432	-.579	.057	-.158	LUNG 19,693 49,999	.371	-.521	.047	-.145	<25 260,453 26,615	.409	-.534	.058	-.147
HDHP 140,309 19,438	.433	-.568	.056	-.145	LYMPHOMA 73,116 55,626	.404	-.535	.053	-.145	26-45 909,692 145,933	.437	-.605	.056	-.143
Marketshare					NONCOLON 48,551 104,350	.327	-.464	.053	-.145	46-65 2,817,160 455,551	.428	-.601	.055	-.149
<1% 18,167	.435	-.634	.054	-.146	NONSPEC 48,698 65,176	.374	-.507	.052	-.146	**DRUG**				
1-5% 33,755	.427	-.652	.055	-.146	PROSTATE 34,942 18,064	.492	-.674	.058	-.148	OS≤3 456,928 288,919	.417	-.456	.060	-.147
5+% 23,310	.424	-.603	.055	-.144	SECOND 113,446 140,801	.378	-.523	.052	-.145	OS>3 3,530,377 344,776	.431	-.616	.052	-.148
					SKIN 205,588 40,031	.427	-.587	.057	-.147	Distinct Cos. <8 companies	.395	-.550		
					TESTES 1,509 954	.414	-.598	.049	-.148	Distinct Cos. ≥8 companies	.449	-.620		
					URIN 18,125 35,923	.414	-.582	.047	-.145					
					UTERINE 58,865 20,309	.398	-.565	.052	-.148					

Table 3.4: Regression Results Pay Differences

	Model 1		Model 2		Model 3		Model 4		Model 5	
	Single Source	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**
N	626,757	4,025,593	638,696	4,025,674	626,757	4,025,593	66,034	384,061	64,849	384,061
Year	0.0040***	-0.1050***	0.0031***	-0.0677***	0.0040***	-0.1050***	0.0048***	-0.0560***	0.0054***	-0.1008***
Comp	-0.0108***	-0.0094***	-0.0097***	-0.0032***	-0.0108***	-0.0094***	0.0057	0.0438**	0.0044	0.0358**
EPO	-0.0172***	-0.0220***	-0.0172***	-0.0257***	-0.0172***	-0.0220***	0.0191**	0.0895***	0.0208**	0.1039***
HMO	-0.0211***	-0.0046***	-0.0208***	-0.0054***	-0.0211***	-0.0046***	-0.0037	0.0409**	-0.0027	0.0469***
POS	-0.0105***	0.0006	-0.0102***	0.0001	-0.0105***	0.0006	-0.0084	0.0683***	-0.0081	0.0690***
PPO	-0.0169***	-0.0069***	-0.0166***	-0.0066***	-0.0169***	-0.0069***	0.0019	0.0236	0.0026	0.0273*
PPOCAP	-0.0137***	-0.0682***	-0.0135***	-0.0684***	-0.0137***	-0.0682***	0.0001	-0.0769***	0.0015	-0.0682***
CDHP	-0.0051***	-0.0001	-0.0048***	-0.0010	-0.0051***	-0.0001	0.0032	0.0171	0.0041	0.0251
HDHP	-0.0178***	-0.0065***	-0.0177***	-0.0093***	-0.0178***	-0.0065***	0.0025	-0.0028	0.0042	0.0075
Marketshare (log)							-0.0021***	0.0094***	-0.0019***	0.0093***
Hourly Employee	0.0059***	0.0132***	0.0059***	0.0135***	0.0059***	0.0132***			0.0034***	0.0110***
Age (log)	0.0085***	0.0460***			0.0085***	0.0460***			0.0062***	0.0563***
Sex	-0.0013***	-0.0152***			-0.0013***	-0.0152***			-0.0031***	-0.0197***
Overall survival >3 months	-0.0102	-0.2263							-0.0180	-0.2497
Years since initial Approval (log)	-0.0072***	1.0652***			-0.0073***	1.0652***			-0.0063***	1.2167***
Number of Unique Manufacturers						0.0083				0.0061
Cons	0.1398***	-2.4692***	0.1536***	0.5525***	0.0996***	-2.6439***	0.1595***	0.3957***	0.1598***	-3.1002***

*p<0.05, **p<0.01, ***p<0.001

Table 3.5: Regression Results Pay Dispersion

	Model 1		Model 2		Model 3		Model 4		Model 5	
	Single Source	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**	**Single Source**	**Multi Source**
N	626,757	4,025,593	638,696	4,025,674	626,757	4,025,593	66,034	384,061	64,849	384,061
Year	0.0223***	-0.0765***	0.0724***	-0.0035***	0.0223***	-0.0765***	0.0589***	0.0111***	0.0223***	-0.0562***
Comp	0.0101***	0.0270***	0.0094**	0.0336***	0.0101***	0.0270***	0.1039*	0.0627***	0.1077*	0.0554***
EPO	-0.0010	0.0270***	-0.0044	0.0226***	-0.0010	0.0270***	0.0788	0.0239	0.0844	0.0313
HMO	-0.0128***	0.0298***	-0.0157***	0.0295***	-0.0128***	0.0298***	0.0901	0.0518**	0.1006*	0.0512**
POS	-0.0095***	0.0304***	-0.0115***	0.0299***	-0.0095***	0.0304***	0.0683	0.0804***	0.0757	0.0821***
PPO	-0.0123***	0.0254***	-0.0152***	0.0268***	-0.0123***	0.0254***	0.0920*	0.0635***	0.0998*	0.0630***
PPOCAP	-0.0177**	0.0263***	-0.0226***	0.0248***	-0.0177**	0.0263***	0.1010*	0.0320	0.1083*	0.0356*
CDHP	-0.0048***	0.0302***	-0.0127***	0.0295***	-0.0110***	0.0302***	0.0979*	0.0532**	0.1045*	0.0587***
HDHP	-0.0110***	0.0325***	-0.0315***	0.0305***	-0.0283***	0.0325***	0.1111*	0.0463**	0.1165*	0.0490**
Marketshare (log)							-0.0035	-0.0062***	-0.0019	-0.0072***
Hourly Employee	0.0059***	0.0008*	-0.0032**	0.0007	-0.0032**	0.0008*			0.0143***	-0.0121***
Age (log)	0.0194***	0.0394***			0.0194***	0.0394***			0.0057	0.0482***
Sex	-0.0162***	-0.0125***			-0.0162***	-0.0125***			-0.0052	-0.0137***
Overall survival >3 months	-0.0815	-0.0508								
Years since initial Approval (log)	0.4178***	2.0839***			0.4178***	2.0839***			0.3029***	1.8568***
Number of Unique Manufacturers						0.0730				0.0780
Cons	-3.7935***	-7.4944***	-3.3087***	-1.5224***	-3.8312***	-7.9081***	-3.4032***	-1.5466***	-3.7938***	-7.3254***

*p<0.05, **p<0.01, ***p<0.001

CHAPTER 4

TRENDS IN US CANCER DRUGS AND IMPACT OF PRICE DISCRIMINATION

KEY TAKEAWAYS

1. The cancer drug market obeys few economic principles.
2. Prices for single source US cancer drugs rose sharply from 2010 to 2014, with AWP increasing 76%, transaction prices increasing 74%, while patient cost sharing increasing 29%.
3. There was significant variation in the increases in AWP and transaction prices across the cancer drugs.
4. The gap between the 10^{th} and 90^{th} percentile for prices increased 159% between 2010 and 2014, widening to $474 in 2014.
5. Plans with capitation had their transaction prices grow marginally slower than non-capitation plans, although the difference was not statistically significant.
6. Four cancer drugs that transitioned to generic saw 9.4% decrease in transaction prices and 5-fold increase in dispersion
7. For each additional manufacturer participating in the multi-source cancer drug market, utilization increases 15.5% and prices surprisingly increase by 3.6%.
8. After controlling for cost, a 10% change in price dispersion increases utilization by 1.1%, suggesting price discrimination in the US cancer drug market can increase access slightly.

4.1 Abstract

This chapter uses longitudinal data to quantify pricing trends of US cancer drug market and assesses the relationship between price discrimination and access. The prices for antineoplastic agents therapeutic class drugs in a large commercial claims database from 2010-2014 are analyzed. For single source drugs, Average Wholesale Price increased 76%, transaction prices paid increased 74%, and patient cost sharing increased 29%. For multi-source drugs, the AWP increased only 6% while transaction price increased 93%. These results are surprising and reflect the fact that cancer drug prices do not follow basic economic principles. A more nuanced analysis suggests that a few cancer drugs distort the relationship between AWP and transaction price growth and are responsible for the anomalies. The gap between the 10^{th} and 90^{th} percentile paid for a single source cancer drug increased from $183 to $474 suggesting increased dispersion. For multi-source, the gap increased from $37 to $55. Plans with capitation grew 4.3% annually while non-capitated plans saw prices paid increase 5.7%.

This study uses a linear mixed methods regression model with random effects and cluster variable around drug to analyze the impact of price discrimination in the US cancer drug market. Results for branded drugs suggest a 10% increase in price dispersion is associated with a utilization increase of 1.1%. For multi-source drugs, the association of price dispersion and utilization was similar, but not statistically significant. Within the multi-source market, each additional manufacturer is associated with a 15.5% increase in utilization.

4.2 Background

Researchers have documented price dispersion for pharmaceuticals across countries[212 213] and within countries.[214 215] This price dispersion has been attributed to pharmaceutical company's ability to price discriminate. Economists define price discrimination as the ability of a firm to set different prices for the same product. This can only occur under three necessary conditions:[216]

1. A firm must be able to act as a price setter, such that an individual firm's demand curve is downward sloping akin to an aggregate market demand curve
2. A firm must control the sale of its product
3. A firm must be able to sort consumers by their demand (different demand elasticities for a drug)

The previous chapters have provided background and discussion of price discrimination in the US cancer drug market. In Chapter 2, there is a discussion on the current literature on price discrimination and a conceptual model relating the five key actors in the US cancer drug market (patients, payers, physicians, drug manufacturers, and the government). Chapter 3 uses the conceptual model developed in Chapter 2 and theories on price discrimination in markets with imperfect competition to empirically analyze a US commercial claims database for price discrimination in the US cancer drug market. The results of Chapter 3 suggest evidence for price discrimination. This chapter builds upon this prior work by quantifying pricing trends in the US cancer drug market and assessing the impact of price discrimination in the US cancer drug market. These goals

[212] Danzon, P. M., & Chao, L. W. (2000).
[213] Lichtenberg, F. R. (2010).
[214] Frank, R. G. (2001).
[215] Lichtenberg, F. R. (2010).
[216] Varian, H. R. (1989).

are motivated by current research on pricing trends in the US cancer drug market and research on the impact of price discrimination.

High drug prices have been discussed much recently by policy makers and researchers alike; and cancer drugs are no exception. Several researchers have suggested that cancer drug prices in the US are exceptionally high with little association with the value of the drug.[217] [218] This is shown in the prior chapter. Other researchers have also observed an upward trend in cancer drug prices.[219] Researchers have examined pricing trends based on average wholesale price (AWP), transaction price, and wholesale acquisition cost. Much of the research has been descriptive focusing on pricing trends; there have been both quantitative and qualitative attempts to explain the increased price trend of cancer drugs.

Howard et al suggest that the price trend is related to "reference pricing", which stipulates that the price of each new drug is based on existing drug prices plus a premium.[220] They also speculate that the price trend does not have a demand side (increase demand for cancer drugs) or supply side (fewer sellers of drugs) response. This chapter will add to current research by examining price trends for cancer drugs. It will also examine other trends including changes in price dispersion, difference between AWP and transaction price, gap between the 10^{th} and 90^{th} percentile of prices for the same drug, utilization, and changes to supply manufacturers in the 2010 to 2014 time period. These results will serve as the foundation for the assessment of the longitudinal impact of price discrimination in the US cancer drug market.

[217] Elkin, E. B., & Bach, P. B. (2010).
[218] Kantarjian, H. M., Fojo, T., Mathisen, M., & Zwelling, L. A. (2013).
[219] Dusetzina, S. B. (2016).
[220] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).

For economists, price discrimination invokes judgment based on the impact on welfare. Welfare is a measurement of the utility a particular good or service provides, and typically measured in currency units such as dollars. [221] Currency, including dollars, provides researchers a measurement of value that is assumed indifferent between individuals versus corporations since both value dollars. This allows a measurement of welfare that can aggregate both the producer surplus (i.e. price sold and cost) and the consumer surplus (i.e. difference between price paid and willingness to pay). In general, according to some economists, if price discrimination increases output, then it increases welfare.[222]

While price discrimination may improve welfare by increasing output according to economists, it is not a Pareto optimal improvement since some consumers will be worse off as their consumer surplus is transferred to the producer.

Moving from theory to the drug market, Danzon,[223] Lichtenberg,[224] and Malueg and Schwartz[225] all have argued that price discrimination improves welfare. The crux of their argument is price discrimination enables drug manufacturers to enter markets that normally would have market prices below a pharmaceutical's uniform market price. They reason that pharmaceuticals need prices high enough to recoup the relatively large fixed costs associated with the research and development of pharmaceuticals. In a uniform pricing market, prices that are high enough to incentivize research and development would be too high for many markets, thereby limiting output and welfare.

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[221] Arrow, K. (1962).
[222] Danzon, P. M. (1997).
[223] Danzon, P. M. (1997).
[224] Lichtenberg, F. R. (2010).
[225] Malueg, D. A., & Schwartz, M. (1994).

The implication that output is related to welfare is crucial for policy makers since increased output may suggest improved access; this will be further discussed.

Most of this discussion of the welfare gain associated with price discrimination is in the international context, with markets being defined by countries. Despite suggestions of price discrimination in the US, there is little economic analysis on whether price discrimination is good or bad in the US. With that said, one could argue that differential prices benefit society by allowing budget sensitive purchasers such as Medicaid or the Veterans Administration access to drugs at lower prices than other purchasers thereby suggesting improved access. However, not all groups benefit under differential pricing in the US, notably the uninsured who pay the highest prices in the US.[226]

For US policy makers, access is a major concern; whether US patients can access appropriate drugs and treatments. This concern has underpinned many of the major health policies in the US, such as the Patient Protection Affordable Care Act. This is a different concern from the economist's view of welfare gains. Whether price discrimination in the US cancer drug market improves access by allowing cancer drugs to be more favorably placed on formularies is the main criterion for assessing the impact of price discrimination in the US cancer drug market. Secondary to access, policy makers are also concerned with the equity and fairness of price discrimination in the US cancer drug market. Under price discrimination, some patients either through premiums or co-pays will pay more than other patients. This should be a significant concern for policy

[226] Frank, R. G. (2001).

makers especially within the US where significant inequities exist[227] and health plans are typically tied to employment that restricts patient choice.

In Chapter 3, results shown the difference between the 10th and 90th price paid in single source drugs is $300 and >$500 for many high priced drugs. For policy makers it is important to know if price dispersion is static or growing? Are certain health plan types more consistently accessing lower prices? Both questions are motivated by concerns of inequity under price discrimination. Price discrimination also raises questions on fairness since it represents a transfer of consumer surplus to drug companies in the form of higher profits. This welfare transfer needs to be contrasted against increased access.

This chapter quantifies pricing trends in the US cancer drug market. By quantifying trends, the chapter highlights areas that are of concern for policy makers. The trends also provide data to test for increased utilization (as noted earlier, a proxy for welfare improvement) associated with price discrimination. Trends analyzed include changes in the AWP, total transaction price, cost sharing of patients, the gap between the 10th and 90th percentile of prices paid for the same drug, and levels of price dispersion and discounts for US cancer drugs in the US cancer drug market. The project will then use these pricing trends to assess the impact of price discrimination in the US cancer drug market. This will be done by analyzing changes in price dispersion and associated changes to drug utilization in the US cancer drug market. The primary hypothesis is that price discrimination is associated with utilization of cancer drugs in the US commercially insured market. In addition, the study examined four secondary hypotheses. These are:

[227] Davis, K., & Ballreich, J. (2014).

1. The gap between the 10th and 90th percentile price paid for a drug will increase.
2. Health plans with capitation will see slower rates of price increases.
3. Following the transition from branded to generic drugs, cancer drugs will lower their prices, have greater dispersion, and increased use.
4. For generic cancer drugs, an increase in number of participating manufacturers will be associated with lower prices, higher dispersion, and increased utilization.

The primary and four secondary hypotheses will be tested with regression models using commercial claims database from 2010-2014. The results and policy implications will be discussed.

4.3 Data

The study quantifies pricing trends in the US cancer drug market and uses these trends to assess the impact of price discrimination in the US cancer drug market. The data is from the Truven Health MarketScan® Research Database (MarketScan®) from 2010 to 2014 supplemented with Truven Health Red Book®. MarketScan® contains insurance claims for nearly 66 million Americans who have employer-sponsored health insurance. The key data file from the MarketScan® database was the drug outpatient claims data file. The Red Book® file provided additional information regarding drug manufacturers on cancer drugs. Additional discussion of the analytic file is in Chapter 3.

Cancer drugs and their corresponding National Drug Codes (NDCs) were identified using the antineoplastic therapeutic class indicators (therapeutic classes: 21, 251, 260, 261, 262, and 263) within the Red Book® data set. The NDCs were matched

to the MarketScan® Outpatient Drug claims, and drugs were excluded if they had less than 100 observations and less than $1 million in sales over the study time period.

The drugs were categorized as "single source" or "multi-source" or "new generics". Single source where drugs that were either branded, which meant they were patented or had marketed exclusivity, or the drugs were single source generics and faced no generic competition. Multi-source includes both multi-source generics and single source brands with generics. For "single source" and "multi source" designations were based on their generic indicator in Red Book®. The "new generics" included four drugs that started as branded drugs, but lost market protection during the study time period. These four were exemestane (generic approved April 2011[228]), anastrozole (generic approved June 2010[229]), letrozole (generic approved June 2011[230]), and capecitabine (generic approved September 2013[231]). These four drugs provide a unique situation to temporally test the relationship between loss of market protection, price discrimination, and changes to price and utilization. Across the full sample, there were 62 unique drugs; 112 unique drugs when considering different dosages and forms.

The MarketScan® Outpatient Drug claims provide detail for each prescription claim by enrollee. The claim lists the service date NDC, Average Wholesale Price (AWP), number of units dispensed, payment from the insurer, payment from the enrollee, and other variables. Similar to the analysis in Chapter 3, an AWP per unit variable was

[228] https://www.drugs.com/availability/generic-aromasin.html [ACCESSED Feb 2, 2017]

[229] https://www.drugs.com/availability/generic-arimidex.html [ACCESSED Feb 2, 2017].

[230] https://www.drugs.com/availability/generic-femara.html [ACCESSED Feb 2, 2017].

[231] https://www.drugs.com/availability/generic-xeloda.html [ACCESSED Feb 2, 2017].

created. The AWP price serves to define the reference unit. The variable of interest is the price dispersion for each drug, akin to the key dependent variable in Chapter 3, but adjusted for the longitudinal nature of the data. Drug was defined by the generic indicator, which indicates bioequivalent drug. For single source drugs, each dose had its own generic indicator, regardless if they were branded or single source generic. For multi-source drugs, the generic indicator linked all the generically equivalent NDCs.

Price dispersion was calculated as the coefficient of variation of transaction prices within the AWP per unit transactions defined in Chapter 3. This variable was transformed to adjust for the longitudinal nature of the data using Equation 1. The price dispersion variable was averaged across all transactions for drug *i* during month *t*.

EQ 1 $$Pdisp_{i,t} = \frac{\sum \frac{P(std)}{\bar{P}}}{fills}$$

The dependent variable is utilization that is based on the total number of fills for each drug *i* during month *t*. The variable was calculated using MarketScan® Outpatient Drug claims with Equation 2.

EQ 2 $$Totfills_{i,t} = \sum fills$$

For quantifying the price trends and answering the secondary hypotheses, several other variables were created using the analytic file. There were five price variables of interest. These variables include AWP, transaction price, patients cost sharing, prices paid by plans with capitation, and prices paid by plans without capitation. All five price variables were calculated as the average across each transaction for each drug *i* during month *t*. Health plans were categorized as plans with capitation for based on the plan

type. Plans that were considered Health Maintenance Organizations (HMOs) or Point-of-Service (POS) plans with capitation were considered plans with capitation; the remaining plans were considered not capitation. A discussion of the plan types is in Chapter 3.

These five price variables were of interest because they reflect prices paid by the two main consumers for in the US cancer drug market: the health plan and the patient. AWP was included because prices paid are ultimately discounted off of the AWP. It is a price that is the starting point for all negotiations and does not vary by market. The prices paid by health plans were of interest because there is a growing trend of declining market share by health maintenance organizations (the primary plan with capitation).[232] Given that HMOs tend to have higher premiums but more generous coverage, this trend could result in growing inequity in the quality of coverage of people covered by employer-sponsored insurance.

There were two calculations for the price trends of the five variables of interest. The first method was to look at average prices in the first half of 2010 and compare that to the average prices in the second half of 2014. This method does not take into consideration changes to the market basket of drugs. Because drugs enter and exit the market and because price could affect the demand for drugs, this is an imperfect comparison. The second, alternative method, was to look at price trends based on average monthly changes. The average monthly change in price would then be compounded over 12 months to determine an average annual price change. The second method is known as the adjusted price trend and described in Equation 3.

[232] Claxton, G., Rae, M., Panchal, N., Damico, A., Whitmore, H., Bostick, N., & Kenward, K. (2013).

EQ 3 $Annual\ Price\% =$

$e^{\frac{\sum \log(\frac{p_t}{p_{t-1}})}{T}}, where\ T\ is\ total\ months\ drug\ is\ on\ market$

Both methods have benefits and drawbacks. The unadjusted price trend will be more applicable to patients and health plans as they would focus on the bottom line of drug spending. However, the price change for the full sample could be biased since the drugs in the first half of 2010 lineup are different from the drugs in the second half of 2014. The adjusted price trend takes into consideration the change in the cancer drug sample. The adjusted price trend is calculated by averaging the monthly price change for each drug. The average monthly price change is compounded to estimate the annualized change. This method weighs each drug equally whether the drug entered the market from 2013-2014 or was on the market throughout the entire study sample since it calculates the annualized price change on average monthly price changes. The adjusted price trend addresses the bias in the first method. Table 4.1 presents results for the unadjusted and adjusted price trends.

The other key variable for of interest is the number of distinct manufacturers per drug per month. This variable was created by linking the MarketScan® Outpatient Drug claims to Red Book® using each transactions NDC. The Red Book® file provided the responsible manufacturer for each NDC. This allowed for a count of unique manufacturers for each drug (defined by generic indicator) for each month. This variable is of interest because prior research has suggested an association between prices and number of manufacturers within the generic drug industry.[233] This project will go beyond

[233] Frank, R. G., & Salkever, D. S. (1997).

prior research by looking at the role of the number of manufacturers and not only price but also dispersion and utilization. Note that this analysis is only conducted in the multi-source drug sample since by definition single source drugs all have one manufacturer.

4.4 Methods

The primary null hypothesis is that price discrimination is unrelated to changes in utilization cancer drugs in the US commercially insured market. This hypothesis examines whether price discrimination increases utilization and by extension access. Additionally, under the assumption that an increase in output increases welfare, the rejection of the primary hypothesis would suggest that price discrimination increases welfare within the US cancer drug market. To test this hypothesis, the study will take advantage of the longitudinal nature of the dataset. Specifically, it will measure utilization as number of monthly fills for each drug. This dependent variable will be regressed against variables for price dispersion (proxy for price discrimination), price, percent discount to AWP, time trend, and in the case of multi-source drugs, number of manufacturers. Analyses of the other variables discussed in the data section will relate to the four secondary hypotheses.

Before the testing of the primary and secondary hypotheses, data cleaning and variable preparation was undertaken. For data cleaning, the same processes were used in this study as was described in Chapter 3. The data cleaning addressed the outliers in the data. Variable preparation included examining the distribution of variables and log transform when necessary, and variable creation as discussed in the data section.

4.4.1 Primary Hypothesis Model

The primary hypothesis will be tested by measuring changes in fills and regress this outcome variable against changes in price, price dispersion, price discount, and a time variable to account for time trends. The data was panel data with the time month, and id is generic id. Both the use of lagged and simultaneous independent variables were explored. The reasoning for using lagged independent variables was to reduce simultaneity bias; however, the serial correlation of the variable suggests that bias would still be present. The reasoning for using simultaneous independent variables is that decisions on drug demand would be done concurrently with price changes. Both models produced similar results, but the intuitive reasoning for using simultaneous independent variables with stronger than the reduction of simultaneity bias; therefore, simultaneous variables are shown in the tables. Refer to Equation 4 for model.

EQ4. $$LOGFILLS_{i,t} = \beta_0 + \beta_1 LOGPRICE_{i,t} + \beta_2 LOGDISP_{i,t} + \beta_3 P.DISC_{i,t} + \beta_4 t_i + U_{i,t} + \varepsilon_{i,t}$$

The dependent variable is the log of fills for drug *i* at month *t*. The independent variables is the log of price, log of price dispersion, and amount of price discount for drug *i* at month *t*. A variable for the time trend was also included. Clustered standard errors were used to account for clustering of standard errors around each drug. Random effects would produce different levels of standard errors for each drug, and un-clustered errors would bias coefficient estimates towards statistical significance.

The model was tested for both fixed and random effects, which typically is done with the Hausman test, but in this case, the test used was the Sargen-Hansen test due to

unbalanced panel data. The data was considered unbalanced for either new drugs entering the market drugs or because drugs were discontinued during this time period. Because there was no uniformity of which drugs are filled during each month; there was unbalanced panel data.

All variables except for price discount were log transformed due to the skewness. The results were then untransformed through exponents for coefficient interpretation. For situations where the independent and dependent variable were both log transformed, the coefficient of the independent variable was the exponent for the corresponding percentage change. For situations where the dependent variable was log transformed and independent variable was not, the coefficient independent variable was exponent for the mathematical constant *e*, with the results interpreted as percent change.

As with any econometric model, there is a concern of endogeneity. For this model, endogeneity may exist between the price dispersion and drug utilization. The theory assumes that increased price dispersion increases utilization. However, price dispersion could decrease utilization if drug companies used price dispersion to counter a decreased demand for drug amongst select health plans. In essence, the drug company could cut prices to stimulate demand if the rates of utilization of a drug for specific health plan were underperforming. This is speculative, but serves as an example of possible endogeneity. The sign, magnitude, and significance of the log of dispersion variable will be suggestive of the impact of price discrimination.

4.4.2 Secondary Hypotheses Models

The first secondary null hypothesis is that the gap between the 10th and 90th percentile price paid for a drug will be constant. The measure of the gap between the 10th and 90th percentile price paid can be interpreted as 1) another measure of price dispersion and 2) a measure reflecting growing inequity. For the former, measuring the spread is just another way of measuring how the price varies. However, this measure is absolute and not relative. Drugs with higher prices might have lower relative dispersion, but because of their higher prices the dollar amount of their dispersion could be greater. For the latter, changes to the price gap suggest some plans are getting access to lower prices and other plans are not. Plans with access to lower prices should have lower premiums and this will benefit enrollees. Alternatively the health plans could retain the lower prices and earn additional profits. Higher prices can result in access restrictions either through formulary controls or increased cost sharing of the patient. Regressing the magnitude of the price gap over the study period against a time variable for single source and multi-source drugs separately will assess the secondary hypothesis. It will be examined using the relative and absolute magnitude of the difference. The number of fills for each drug will serve as a weighting for the price gap. The sign, coefficient, and significance of the time variable will either confirm or reject the hypothesis.

The next secondary null hypothesis is that health plans with capitation will see no difference in rates of price increases versus health plans with no capitation. As discussed earlier, a price between health plans with capitation versus health plans without capitation may suggest some enrollees have access to lower-priced drugs over time. Price discrimination would allow prices to be set differently for health plans with capitation

versus health plans without capitation, assuming capitation would affect drug demand. This assumption is reasonable given previous literature on drug spending and demand by HMOs versus other health plan types.[234] This hypothesis will be assessed by comparing the price trends for drugs paid by health plans with capitation versus prices paid by health plans without capitation over time. A t-test will be conducted comparing the price trends for health plans with capitation versus health plans without capitation. This t-test will use a two-sided hypothesis test to check if the trends are statistically different.

The third secondary null hypothesis is cancer drugs that transitioned from branded to generic will not see differences in prices, dispersion, and use. The intuitive reasoning for rejecting the null hypothesis is when a drug goes from branded to generic and more manufacturers enter the market, then the cross price elasticity should increase and result in greater dispersion. The other two aspects of this hypothesis, i.e. lower prices and increased use, have been confirmed in other studies, but not specifically in the US cancer drug market. This hypothesis will not be tested using statistical models but rather descriptive statistics for prices, dispersion, and increased utilization. Descriptive statistics for each drug will be presented for the six months prior to generic entry, followed by six months, one year, and two years after generic entry. A graph depicting changes in AWP, transaction prices, and number of unique manufacturers will be presented for visual analysis for the drug anastrozole.

The last secondary hypothesis concerns multi-source cancer drugs. The null hypothesis is that an increase in number of participating manufacturers is not associated with lower prices, higher dispersion, and increased utilization. Prior research has shown a

[234] Joyce, G. F., Escarce, J. J., Solomon, M. D., & Goldman, D. P. (2002).

relationship between number of generic drug manufacturers and price, with the price effect maxing out at 8 manufacturers, but this analysis will control for other market factors such as price dispersion and utilization. This hypothesis will be tested by including a variable for the number of distinct manufacturers within each drug in the model for the primary hypothesis detailed in EQ 2. The sign, coefficient, and significance of the time variable will either confirm or reject of the hypothesis.

While the statistical models will test most of the proposed hypotheses, descriptive statistics and graphs will present pricing trends for the AWP, transaction price, cost sharing of patients, and price gap for the US cancer drug market

4.5 Results

The study quantifies trends in the US cancer drug market and assesses the impact of price discrimination in the US cancer drug market. Table 4.1 provides descriptive statistics for several important variables over time. Table 4.2 provides the statistics for the unadjusted, adjusted, and by product price trends. The added granularity of Table 4.2 highlights the distribution of price increases across products. Over time, there were significant price increases. Using the adjusted pricing trend, 78 out of 110 drugs experienced positive annualized average AWP increases; 84 out of 110 drugs experienced positive annualized average transaction price increases. Examining just the single source environment, 65 of the 87 drugs had positive AWP increases and 69 of the 87 drugs had positive annualized average transaction price increases. Additionally, 26 single source drugs experienced annualized transaction price increases greater than 10%.

The growth of prices for single source is affirmed by prior research,[235] nonetheless, it is surprising in terms of magnitude. Perhaps most surprising is that nearly a third of single source for cancer drugs experienced annualized price increases greater than 10%. This growth, which far exceeds inflation, could be attributable to higher costs. For pharmaceutical companies, the primary cost is research and development and this is a fixed cost.[236] The R&D costs have been characterized as inherently risky.[237] However, at the industry level, the pharmaceutical company spending on research and development has not gone up significantly since 2010.[238] Further research is needed to explain these significant price increases.

For patients, there was also an increasing trend in cost-sharing during the study time period. Using unadjusted price trends, which more accurately reflect patient expenditures, there was an observed 29% increase in patient cost-sharing in single source drugs, and a smaller 9.6% increase in multi-source drugs. There was also significant seasonality most likely due to patients reaching out-of-pocket deductibles. The average level of cost-sharing spiked in the first two months of the year across all four years. To adjust for seasonality, when calculating the overall trend year-by-year comparisons were made; this approach smoothed out the January and February spikes of cost-sharing.

The relatively slow growth of the increase in cost-sharing is surprising given the increasing trend of more patient financial responsibility within health plan formularies.[239]

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[235] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).
[236] Berndt, E. R., McGuire, T. G., & Newhouse, J. P. (2011).
[237] DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016).
[238] Pharmaceutical Research and Manufacturers of America (PhRMA) Report, "Biopharmaceutical research and development: The process behind new medicines" http://www.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf, 2015.
[239] Joyce, G. F., Escarce, J. J., Solomon, M. D., & Goldman, D. P. (2002).

However, the slow growth in cost-sharing may be an artifact of patients hitting their maximum out-of-pocket expenditures due to other healthcare services for their cancer diagnoses (i.e. hospitalizations). It may also be due to coupons and other patient assistance programs that mitigate the cost-sharing for cancer drug prescriptions, but further research is needed especially using other data sets that delineate the coupons' and patient assistance programs' financial contributions to the patients' cost-sharing expenditures.

The price gap for prices paid between the 10^{th} and 90^{th} percentile for the same drug appears to have increased. For single source drugs, the price gap increases from $183 to $474 representing a 159% increase. For multi-source drugs, the price gap increases from $37 to $55 representing a 50% increase. Clearly, both the absolute and relative growth of the price gap were greater in single source drugs. This may suggest a growing willingness by drug manufacturers to price discriminate in more expensive drugs, and an underlying growing inequity when it comes to expensive medications.

Of particular interest for the primary hypothesis, the level of price dispersion for single source drugs increased 28% during the study period. There was also a minor increase in the discount between AWP and transaction price. Contrasted to the single source results, the multi-source results showed a decrease in both price dispersion and discount between AWP and transaction price. An increase in the transaction price relative to the AWP may suggest a collective increase in market power by generic cancer drug manufacturers. This increase in market power would increase the price, and for drug companies, the transaction price better reflects the actual price rather than the AWP. The increase market power of multi-source cancer drugs may be due to the consolidation

in the generic manufacturer market or a response to higher single source drug prices thereby making generic alternatives more appealing to payers. In this study sample, single source cancer drugs were nearly 50 times the price as multi-source drugs. The fact that the AWP did not change substantially for multi-source drugs may be due to possible unobserved characteristics of multi-source cancer drugs or manipulation of the value of rebates since AWP is often used as the benchmark price for other payers' notably state Medicaid programs.

The primary hypothesis is that price discrimination is not associated with utilization of cancer drugs in the US commercially insured market. Two regression models were used: one with fixed effects for the drug and the other with random effects for the drug. The Sargen-Hansen test indicated a Chi-square with a corresponding p-value of <.0001 for all three models, suggesting a random effects model. Both models were tested across the full sample, single source sample, and multi-source sample.

For the full sample, the coefficient for price dispersion is .114 with a p-value of .001. This tells us that a 10% increase in price dispersion is associated with a 1.1% increase in fills, and this value is statistically significant. For the single source sample, the coefficient for price dispersion is .105 with a p-value of .001, which is estimates a 10% increase in price dispersion is associated with a 1.0% increase in fills. These results suggest a rejection of the null hypothesis that there is no association of price discrimination with utilization; therefore, it appears, at least in single source market, price discrimination of cancer drugs improves access, albeit minimally. For the multi-source sample, the price dispersion coefficient increases to .236 but the p-value also increases to .13 suggesting no statistical significance.

The price and time trend are only significant in the full sample and multi-source subset. Specifically for the multi-source subset, a 10% increase in transaction price is associated with a 5.1% increase in fills. This is counter to traditional economic theory, where lower prices should dictate increase in fills and not vice versa. However, there are two possible explanations. The first and most likely is that the small number of drugs in the multi-source cancer drug market may create perverse results if unobserved factors affecting specific drugs were not accounted in the model. For example, the positive relationship between transaction price and fills could be due to new research on a generic drug in a cancer indication, and manufacturers may respond to the increasing demand (higher fills) with an increase in price. The other alternative is that the multi-source cancer drug market competitive forces are hindered by barriers of entry and regulatory environment. Howard et al suggest that normal supply and demand competitive forces do not work in the cancer drug market.[240] Generic manufacturers can be increasing prices while at the same time experience increased demand due to increased cancer prevalence and/or increased access to treatment. Another explanation lies in the distribution of price and utilization increases across multi-source drugs. Three of the nineteen multi-source drugs experienced annualized price increases greater than 10%, and these three saw increases in utilization while the rest saw small increases or decreases (average of -0.7%). Further research is needed to see why these three saw big increases in price and utilization.

The study results reject the first secondary null hypothesis that the gap between prices paid at the 10th and 90th percentile is unchanged. For single source drugs, the gap

[240] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).

increased from $183-$474 representing 159% increase. This suggests that patients and some health plans will be accessing drugs at prices substantially less than other patients and other health plans. For policy makers, the question is whether this is equitable and fair especially in the US where most people are enrolled through employer-sponsored insurance and have little choice on health plans.

The other secondary hypothesis examines health plans stratified by health plans with capitation and plans without capitation. The null hypothesis is that the trend in prices paid between these plans is not different. Plans with capitation experienced annual price increases of 5.9% versus plans without capitation that experienced annual price increases of 7.0%. The difference of 1.1% is small but could compound significantly over time. However, a t-test rejects the hypotheses that the growth rates are statistically different.

There were four cancer drugs that experience generic competition during the study time frame: exemestane, anastrozole, letrozole, and capecitabine. The null hypothesis is that there would be no change in transaction prices, utilization, or price dispersion when the drugs experience generic competition. The results of the analysis are in Table 4.3 and suggest a rejection of the null hypothesis. All four of these drugs experience considerable decreases in transaction prices of about 9.4% in the first year post-generic entry. There was also a significant increase in price dispersion for these drugs after generic entry. Interestingly, two drugs had sharp decreases in utilization, while the other two drugs had slight increases in utilization. A sample size of four cancer drugs is very limited and results can be biased due to unobserved market forces with these for drugs; this limits generalizability.

The last secondary hypothesis examines the relationship between number of unique manufacturers and price and utilization in the multi-source cancer drug market. The null hypothesis is there is no association between the number of unique manufacturers and drug price or utilization. The analyses to test this hypothesis was similar to the primary hypothesis model, with the exception that to test the relationship between the number of unique manufacturers and drug price the dependent variable of utilization and independent variable drug price were flipped. Results are presented in Table 4.3 in the fourth column.

The results suggest there is a positive relationship between the number of unique manufacturers and utilization. For each new manufacturer, utilization increases 15.4%. The results also suggest a positive statistically significant relationship between the number of unique manufacturers and price; each new manufacturer average transaction price increases 3.6%. Both of these results are contrary to classic economic theory. There are two possible explanations of these results. First, generic drug manufacturers may enter markets where they perceive excess demand and upon entry satisfy the excess demand hence increased utilization. Second, drug manufacturers may induce demand and as a result utilization and prices increase. This argument is weaker in the generic drug market since specific generic drug companies do not have the type of market power that branded drug company would have. The results are contrary to Frank and Salkever[241] who found evidence suggesting more generic manufacturer's lower prices, but this study was older (>20 years) and looked at multiple drug classes.

[241] Frank, R. G., & Salkever, D. S. (1997).

4.6 Limitations

There are two important considerations when using cancer drug claims data. First, as with any pharmaceutical product, there's concern about rebates, chargebacks, and coupons and whether the data set allows us to observe actual prices paid. Rebates and chargebacks has money flowing from the drug manufacturer to the PBM and health plans. Coupons can distort the patient cost-sharing and patient drug demand by reducing the financial incentive to purchase cheaper drug alternatives.

Second, outliers exist, and these outliers may not be representative of the market and can bias results. For example, large price spikes in select drugs or with select health plans can give policy makers the wrong impression on drug price trends. The mechanisms to address outliers are discussed in Chapter 3. For the methods, limitations inherently exist with the regression analyses. These limitations included model misspecification, omitted variable bias, and endogeneity. The model and variable selection could be wrongly specified, this may result in biasness in the estimates. Omitted variable bias is a concern, since other factors such as relative cost of non-drug treatments can influence drug demand via cross-price elasticities or the role of marketing on drug demand which has been shown to effect demand.[242] Endogeneity may exist in the relationship between prices and quantity, which economists tend to encounter. A benefit for using single source cancer drugs is that these drugs have significant market power and the drug manufacturer can be reasonably assumed to be a price setter. Therefore, the relationship between quantity and price is not set simultaneous in the

[242] Berndt, E. R. (2002).

market, rather, prices are set and then the market demand responds. This dynamic is also related to simultaneous bias, and could be more influential in the multi-source market.

The last notable limitation is the limited generalizability of the US cancer drug market to either other therapeutic classes the US or other countries. Cancer is a devastating disease and can be considered either acute or chronic depending on the clinical situation. Other entities, notably the National Institute of Clinical Excellence in England has recognized the uniqueness of the cancer drug market and proscribes cancer drug specific regulations.

4.7 Policy Implications

The chapter produced two sets of analyses: quantifying trends in the US cancer drug market and assessing the impact of price discrimination. Both have policy implications. For the trend data, the study confirms previous studies[243] that have highlighted significant price increases for single source drugs. These price increases far exceeded normal inflation and contribute to the broader discussion of high drug prices in the US.

Beyond validating previous studies, this chapter draws awareness to other concerning trends in the US cancer drug market. First, for single source drugs the gap between the 90th and 10th percentile of prices paid for the same drug has widened at a greater rate than transaction prices and AWP. This suggests that the gap between those who have access to lower drug prices versus those who have access to high drug prices

[243] Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015).

may be widening. It is important to consider this inequity in the context of the US health insurance market. Most health insurance is provided through employer-sponsored insurance, and this may limit for an individual's choice of different health insurance plans. Further analysis in terms of who has access to lower premiums should be conducted, but this was beyond the scope of this project.

Within the multi-source market, prices measured by AWP have stayed reasonably flat in US cancer drugs. However, transaction prices have increased. This study did find the reason for the increase, but a possible explanation may lie in with the lack of disclosure of rebates to either PBM or pharmacy, which would be more likely in competitive markets like the multi-source market. These negotiations are hidden behind confidentiality rules. The growth of the transaction price may indeed reflect a growth in the rebate and growing share of the price going to PBMs. This may warrant policy makers to investigate rebates in the multi-source market for two reasons. First, investigate whether rebates lead to price increases, and second, investigate whether more cancer drug revenue is going to PBMs and what added-value warrants this growth.

For policy makers, an interesting finding is the relationship between manufacturers participating and utilization. For each additional manufacturer, utilization goes up 15%, even when controlling for price changes. For now the result is that for each additional manufacturer average transaction prices go up 3.9%. Further research should look at these results and replicate the methods and other therapeutic classes, since the results are contrary to classical supply and demand theory and previous research. If these results hold up, then policy makers should consider what characteristics of the multi-

source market are hindering the expected market forces such that new manufacturers drive transaction prices down.

The study rejected the primary null hypothesis; this study suggests that price discrimination increases utilization, which was confirmed in the single source drugs albeit a very small magnitude. The results suggest a 10% increase in price dispersion increases utilization by 1.1%. However, it is important to consider this magnitude in the relatively low levels of price dispersion in single source cancer drugs.

Average level of price dispersion for single source cancer drugs is nearly 6% compared to a nearly 40% level of price dispersion for multi-source cancer drugs. A 10% increase in price dispersion would only increase price dispersion for single source cancer drugs to just 6.6%. A 100%, 200% or even 300% increase in price dispersion would still result in a lower level of price dispersion for single source versus multi-source cancer drugs. However, increasing price dispersion by multiple factors will further exacerbate the "winners" i.e. health plans and enrollees of these plans that access lower prices, and "losers" i.e. health plans and enrollees of these plans that access higher prices.

For example, as shown in Chapter 3, imatinib had an average price dispersion level of .05, assuming a linear relationship between price dispersion and utilization, if the maker of imatinib would double price dispersion by charging less to some plans and charging more for other plans, then utilization could go up 11% but the price gap would increase to over $1000. For policy makers, at first this result may seem to support policies to encourage differential pricing in the US, but increases in dispersion inevitably result in inequity. Also, the small magnitude and suggestive evidence that chargebacks and rebates are low in branded cancer drugs, weakens the anti-transparency efforts.

Companies argue against transparency since secretive contracts allow some health plans to better "negotiate" lower prices.

4.8 Conclusion

Single source cancer drugs in the US experience considerable price increases in multiple facets of the price from 2010 to 2014. These price trends affected health plans and patients through higher co-pays. These trends were less in magnitude and statistical significance for the multi-source cancer drug market. The gap in prices paid grew significantly during the study time period. The study confirms that price discrimination may increase access to single source cancer drugs in the US market albeit at a small magnitude of effect. Further research should examine who benefits from these trends, causality of the trends, and whether these methods can be applied to other therapeutic classes beyond cancer.

APPENDIX CHAPTER 4

Table 4.1 Price Trends in the US Cancer Drug Market

Variables	1H[1] 2010	2H 2010	1H 2011	2H 2011	1H 2012	2H 2012	1H 2013	2H 2013	1H 2014	2H 2014	**2010-2014 Change**
AWP (S[2])	4078	4409	4718	5194	5842	6068	6438	6699	6745	7179	**76.0%**
AWP (M)	136	135	135	134	134	132	132	133	136	143	**5.5%**
Price (S)	3503	3796	4039	4442	4991	5181	5476	5673	5742	6100	**74.2%**
Price (M)	37	36	36	35	34	37	51	73	71	71	**92.5%**
Patient Co-Pay (S) [3]	99	73	114	82	121	81	116	79	138	84	**29.0%**
Patient Co-Pay (M)	13	12	13	12	13	12	14	14	15	12	**9.6%**
Price Gap 10-90 (S)	183	192	203	249	288	292	321	395	440	474	**159.1%**
Price Gap 10-90 (M)	37	28	30	28	26	29	52	63	53	55	**50.3%**
Price Dispersion (S) [4]	3.0%	5.5%	4.9%	3.5%	4.6%	2.7%	6.5%	4.0%	4.9%	6.0%	**28.1%**
Price Dispersion (M)	30.8%	27.8%	37.4%	34.3%	27.8%	34.9%	50.0%	36.1%	19.4%	33.5%	**-9.6%**
Price Discount (S)	13.8%	13.5%	14.4%	13.9%	14.3%	14.1%	15.0%	14.9%	14.3%	14.8%	**6.3%**
Price Discount (M)	23.7%	45.8%	59.7%	62.5%	43.0%	55.8%	55.8%	45.5%	26.4%	35.6%	**-10.8%**

All variables are in US $ unless otherwise noted.

1. 1H=1st Half, variables are averaged from Jan-Jun
2. S indicates Single Source, M indicates Multi-Source
3. Patient co-pay increases were calculated by comparing average across the first and fifth years
4. Price dispersion increases were targeted by comparing average across the first and fifth years

Table 4.2 Adjusted and Unadjusted Price Trends

Single Source			Multi Source		
	AWP	**PAY**		**AWP**	**PAY**
Unadjusted Annual Change (%)	12%	11.7%	Unadjusted Annual Change (%)	1.1%	14%
Adjusted Annual Change (%)	7.3%	7.4%	Adjusted Annual Change (%)	3.8%	9.1%
By product			**By product**		
AFINITOR	8.7%	8.6%	BICALUTAMIDE	-2.7%	-4.1%
AVASTIN	-4.3%	-4.7%	CYCLOPHOSPHAMIDE	-3.8%	5.6%
BOSULIF	-2.8%	-3.8%	ETOPOSIDE	8.7%	5.2%
CAPRELSA	4.8%	4.3%	LEUPROLIDE ACETATE	-13.1%	-4.5%
COMETRIQ	36.5%	43.5%	MEGESTROL ACETATE	1.6%	1.2%
ERIVEDGE	0.4%	0.6%	MERCAPTOPURINE	3.1%	0.6%
FARESTON	16.5%	16.2%	METHOTREXATE	-1.8%	21.5%
GILOTRIF	-0.1%	2.0%	METHOTREXATE NA	9.5%	22.2%
GLEEVEC	14.5%	14.1%	TAMOXIFEN CITRATE	-3.3%	0.5%
HERCEPTIN	12.1%	10.2%	TEMODAR	50.1%	61.0%
HYCAMTIN	-10.1%	-7.5%	TEMOZOLOMIDE	-6.1%	-9.7%
ICLUSIG	18.6%	22.2%			
IMBRUVICA	-5.4%	-7.7%			
INLYTA	2.4%	3.2%			
LUPANETA PACK	0.0%	1.1%			
LUPRON DEPOT	6.7%	7.0%			
MATULANE	-7.2%	-7.5%			
MEGACE ES	6.6%	6.3%			
MEKINIST	4.8%	6.3%			
NEXAVAR	9.0%	8.5%			
POMALYST	4.6%	5.6%			
RITUXAN	5.9%	5.6%			
SPRYCEL	6.9%	7.1%			
STIVARGA	4.3%	4.3%			
SUTENT	12.7%	12.6%			
TAFINLAR	3.8%	3.2%			
TARCEVA	11.5%	11.7%			
TARGRETIN	31.5%	41.5%			
TASIGNA	4.6%	4.5%			
TEMODAR	12.9%	11.8%			
TEMOZOLOMIDE	-32.1%	-44.2%			
TREXALL	7.7%	6.4%			
TYKERB	8.6%	8.1%			
VALCHLOR	86.0%	84.0%			
VELCADE	-17.6%	-18.9%			
VOTRIENT	7.5%	7.3%			
XALKORI	10.1%	10.6%			
XTANDI	4.5%	4.2%			
ZELBORAF	-1.6%	-1.9%			
ZOLINZA	10.2%	10.1%			
ZYKADIA	2.8%	2.6%			
ZYTIGA	10.4%	10.6%			

Figure 4.1: Price Trends

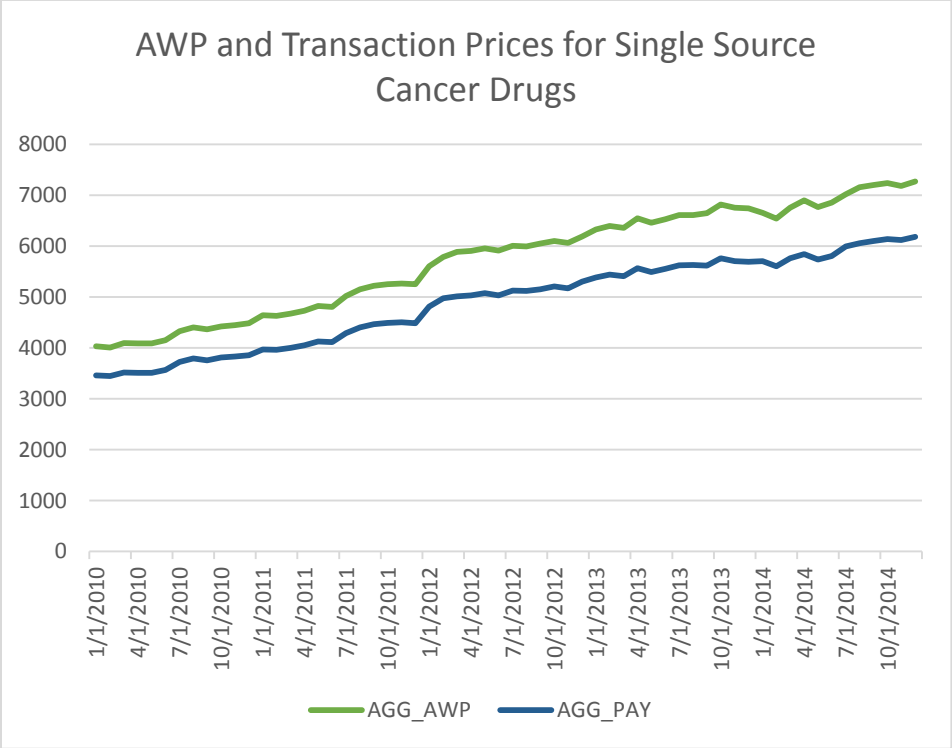


Table 4.3: Primary Hypothesis Model Results

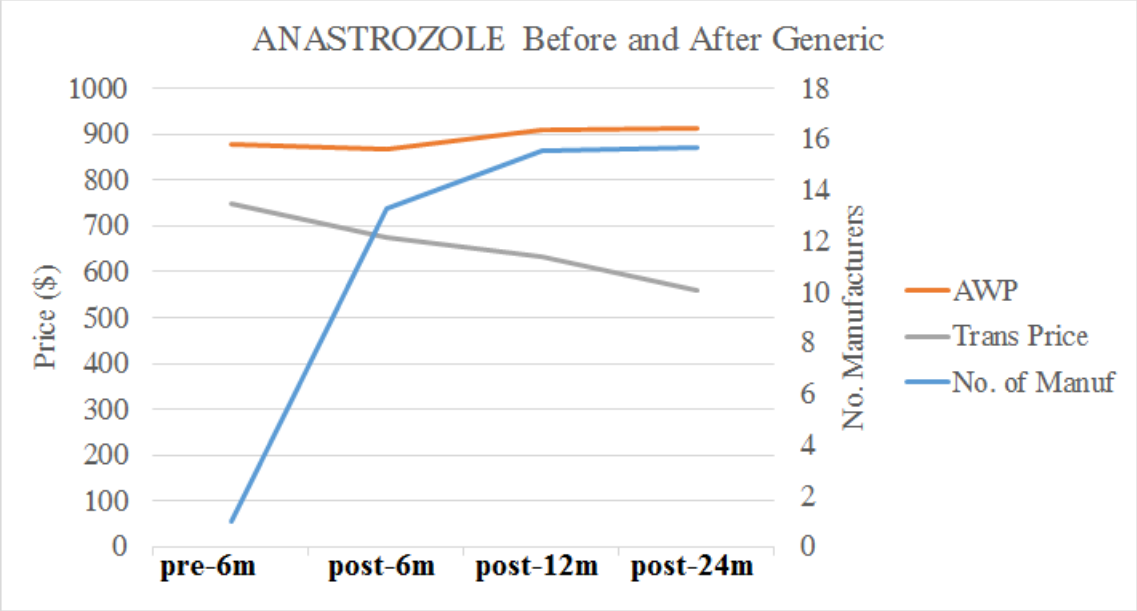
	Full Sample	Single Source	Multi-Source	Multi-Source w/Manufacturer
Log Price	.206*	-.029	.507***	.419***
Log Dispersion	.114***	.105***	.236	.231
Discount	-.358	-1.692	.278	.221
Time trend (month)	-.006*	.0004	-.014***	-.013***
Constant	6.425***	4.150**	12.211***	10.913***
Number of Manu.				1.039***
Model Diagnoses				
R^2 within	.042	.012	.210	.264
R^2 between	.162	.155	.030	.134
R^2 overall	.165	.055	.105	.107
Wald Chi^2	18.29***	10.82**	18.44***	18.11***
Observations	4,761	3,399	1,062	1,062

Test Statistics are based on clustered standard errors around generic product ID (*generid*)
* p<0.10, **p<0.05, ***p<0.01

Table 4.4: Trends after Generic Entry

Drug	Variable	6 Month Prior	6 Month After	12 Month After	24 Month After
EXEMESTANE	AWP ($)	899.09	907.53	905.82	958.37
	Trans Price ($)	674.92	627.30	566.65	574.96
	Price Disp.	0.06	0.17	0.21	0.27
	No. of Manuf.	1.00	3.00	3.00	3.00
	Fills	2331.50	2441.57	2709.69	2675.23
ANASTROZOLE	AWP ($)	879.59	868.14	911.20	911.27
	Trans Price ($)	748.11	673.27	632.82	560.72
	Price Disp.	0.06	0.37	0.58	0.56
	No. of Manuf.	1.00	13.29	15.54	15.69
	Fills	11561.67	8940.14	4774.15	2454.54
LETROZOLE	AWP ($)	907.65	910.90	908.13	971.71
	Trans Price ($)	669.38	609.83	560.02	592.51
	Price Disp.	0.08	0.29	0.62	0.75
	No. of Manuf.	1.00	8.71	10.23	10.23
	Fills	8921.83	5877.00	3398.15	2293.23
CAPECITABINE	AWP ($)	960.08	983.10	999.33	-
	Trans Price ($)	574.84	607.82	625.15	-
	Price Disp.	0.05	0.05	0.13	-
	No. of Manuf.	1.00	1.00	2.50	-
	Fills	1460.50	1456.29	1582.90	-

Figure 4.2: Trends after generic entry



CHAPTER 5

Conclusion

3.1 Summary

The thesis examines current literature on price discrimination in the US cancer drug market; developed a conceptual model relating the five key actors of the US drug market and price discrimination; evaluated evidence for the presence and type of price discrimination; empirically tested the conceptual model; quantified pricing trends in the US cancer drug market; and assessed the impact of price discrimination in the US cancer drug market.

Chapter 2 introduces the concept of price discrimination in the US cancer drug market. A brief discussion of the theory is followed by a structured literature review. These articles discuss the relationship between price discrimination and market power; the relationship between the five key actors (patient, payer, physician, manufacturer, and government) and demand for drugs; and the pricing of cancer drugs. Results from these articles provides the basis of a conceptual model that depicts the interaction between the five key actors and price discrimination in the US cancer drug market. Four largest associations are 1) the ability of pharmaceutical firms to segment the market and engage

in price discrimination, 2) the ability of pharmaceutical firms to have market power and engage in price discrimination, 3) how health plan characteristics can contribute to market segmentation, and 4) how drug characteristics influence the level of price discrimination. These establish a framework for empirical analysis conducted in Chapters 3 and 4.

Chapter 3 analyzes the US cancer drug market for evidence of price discrimination and empirically examines demand factors depicted by the conceptual model of chapter 2. Theory suggests price discrimination in markets with imperfect competition are characterized with increasing levels of price dispersion as the market becomes more competitive up until firms no longer hold market power. Using this theory, price dispersion is examined in single source and multi-source cancer drug markets in the US. In the single source market, smaller discounts (14.7% versus 60%) and smaller levels of dispersion (5.6% versus 43%) are observed relative to the multi-source market. The smaller discounts validate the assumed lower level of competition in the single source versus multisource market. However, because of the higher prices of single source drugs the absolute levels of price dispersion are greater in the single source drugs.

Chapter 4 uses longitudinal data to quantify pricing trends of US cancer drug market and assesses the relationship between price discrimination and access. This chapter uses the same large commercial claims database from Chapter 3. For single source drugs in 2010-2014, Average Wholesale Price (AWP) increased 76%, transaction prices paid increased 74%, and patient cost-sharing increased 29%. For multi-source drugs, the AWP increased only 6% while transaction price increased 93%. This is due

primarily to a few drugs that had rapid increases in the transaction price. The gap between the 10th and 90th percentile paid for a branded cancer drug increased from $183 to $474 suggesting increased dispersion. Plans with capitation grew 4.3% annually while non-capitated plans saw prices paid increase 5.7%. Using panel models with random effects, results suggest that a 10% increase in price dispersion is associated with a utilization increase of 1.1% in single source drugs. For multi-source drugs, the association of price dispersion and utilization was similar but not statistically significant. Uniquely for the multi-source market, each additional manufacturer is associated with a 15.5% increase in utilization. Dispersion is the result of price discrimination, and evidence suggests it increases access, albeit as a small effect.

5.2 Study Limitations

The thesis has several limitations. First, a literature review could have missed critical articles and understanding price discrimination in the US cancer drug market due to the wrong search strategy or overlooking the abstracts during the screening process. Some of the results of the literature review were based in international markets or drug market outside of cancer drug market. These results may not applicable and were incorrectly synthesized to the conceptual model. The conceptual model was simplified to include five key actors of the US drug market however the simplification omitted other entities involved. These include pharmaceutical benefit management (PBM) companies, wholesalers, and pharmacies. The relationship between these omitted entities and price discrimination may distort the results.

Chapter 3 uses a theoretical foundation as the basis of the primary hypothesis for the presence of price discrimination in the US cancer drug market. The theories by

Borenstein[244] and Holmes[245] may incorrect or inapplicable to the US cancer drug market. The empirical analysis uses a large commercial claims database. There are two important considerations when using cancer drug claims data. First, as with any pharmaceutical product, there is a concern about rebates, chargebacks, and coupons and whether the data set observes actual prices paid. Rebates and chargebacks represent money flowing from the drug manufacturer to the PBM and health plans. Coupons can distort the patient cost-sharing and patient drug demand by reducing the financial incentive to purchase cheaper drug alternatives. Second, outliers exist, and these outliers may not be representative of the market and can bias results. For example, large price spikes in select drugs or with select health plans can give policy makers the wrong impression on drug price trends. The mechanisms to address outliers are discussed in Chapter 3.

Both Chapters 3 and 4 use regression analysis to evaluate the hypotheses. Regression analysis has inherent weaknesses including the wrong model specification, omitted variable bias, and endogeneity. All of these can bias the results both sides magnitude of the coefficients as well as statistical significance.

The last notable limitation is the limited generalizability of the US cancer drug market to either other therapeutic classes the US or other countries. Other entities, notably the National Institute of Clinical Excellence in England has recognized the uniqueness of the cancer drug market and proscribes cancer drug specific regulations.

[244] Borenstein, S. (1985).
[245] Holmes, T. J. (1989).

5.3 Study Strengths

The thesis has several study strengths. First, the thesis begins with a structured literature review that errs on more generalness rather than specificity with the search strategy. As evident in the number of identified articles in the initial screening, this strategy minimizes the risk of missing articles. Another study strength was with the development of the conceptual model. Most of the relationships were already clearly defined in literature, which reduce the need to speculate on the associations between the five key actors and price discrimination in the US cancer drug market.

The empirical analysis of the thesis has several strengths. The primary data source is the Truven Health MarketScan® Research Database (MarketScan®) from 2010 to 2014. This database is professionally collected and managed. The database is also large, representing nearly 66 million Americans with employer-sponsored health insurance. While the database is not geographically weighted using standard survey techniques, there is significant geographic variation in observations. Another benefit of the database is the longitudinal nature. By examining multiple years of the US cancer drug market, the thesis was able to test multiple dynamics and not just rely on cross-sectional analysis. Lastly, using a variety of methods including univariate analysis, regression analysis, and graphical analysis, the thesis provides several different ways to examine price discrimination in the US cancer drug market.

5.4 Policy Implications

Results from the empirical analysis in Chapter 3 and 4 provide evidence that price discrimination exists and the US cancer drug market. Danzon,[246] Lichtenberg,[247] and Malueg and Schwartz[248] all have argued that price discrimination in pharmaceuticals improves welfare. The crux of their argument is price discrimination enables drug manufacturers to enter markets that normally would have market prices below a pharmaceutical's uniform market price. They reason that pharmaceuticals need prices high enough to recoup the relatively large fixed costs associated with primarily the research and development of pharmaceuticals. In a uniform pricing market, prices that are high enough to incentivize research and development will be too high for many markets, thereby limiting output and welfare. The implication that output is related to welfare is crucial for policy makers since increased output may suggest improved access.

The analysis in Chapter 4, does suggest that price discrimination increases access in the single source drug market. However, this result carries two key caveats. First, the analysis suggest a relationship in which a 10% increase in dispersion, a proxy for price discrimination, increases utilization by 1.1%. This is not a significant magnitude. While the small magnitude affirms the notion of price discrimination improves access, it may not warrant major support for price discrimination by policy makers. The second caveat is that price discrimination exists because of imperfect competition in the marketplace. Policymakers are partially responsible for imperfect competition through enactment of policies that hinders the free-market. For example, the US has enacted the Prescription

[246] Danzon, P. M. (1997).
[247] Lichtenberg, F. R. (2010).
[248] Malueg, D. A., & Schwartz, M. (1994).

Drug Marketing Act (PDMA) of 1987, which significantly limits arbitrage in the US drug market. This law limits the resale of drugs to wholesalers, stipulates wholesale regulations, and further directs state governments to regulate wholesalers.[249] The PDMA also prevents re-importation of pharmaceuticals; therefore, preventing trans-geographic market transactions. Arbitrage is necessary in markets to improve efficiency, which drives lower prices. Trans-geographic drug trade also has been suggested as a means to lower the price of drugs.[250]

Another policy restricting competition in the US cancer drug market is the granting of market protections, either market exclusivities or patents. Pharmaceutical development is a costly business that requires significant investments in research and development.[251] Market protections are in place to incentivize the research and development; however, these protections prevent competitors from creating an identical drug. The lack of other companies from entering a market with true substitutes is the primary reason branded drugs are so high priced relative to generics.

The results suggest price discrimination slightly increases utilization. Above, two caveats on this statement were discussed. In addition to these caveats, policymakers should be concerned about who is better off and worse off because of price discrimination. Price discrimination involves the transfer of consumer surplus to the drug manufacturer in the form of higher profits. This transfer leaves consumers, whether they are patients or health plans, worse off. Since price discrimination involves differential prices, under any price discrimination scheme, some consumers pay more while other

[249] Angarola, R. T., & Beach, J. E. (1996).
[250] Emanuel, E. J. (2012).
[251] DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016).

consumers pay less. Analysis in Chapter 3 suggests some health-plans pay more than others and the middle age (26-45) pay the most for single source drugs. The gaps are more significant in terms of relative differences the multi-source market. In Chapter 4, the trends suggest greater dispersion as the gap between the 10^{th} percentile and 90^{th} percentile has increased over the study time frame.

Evidence suggests price discrimination exists in the US cancer drug market. Researchers and policy makers alike should be aware of differential prices for cancer drugs. The trend of increasing prices and prices differentials suggest further examination.

Supplementary Table 1

SOURCE	VARIABLE	DESCRIPTION
MarketScan® Outpatient Drug claims	ENROLID	Enrollee ID used to link enrollees to outpatient claims
	SVCDATE	Service date indicates day of prescription payment
	NDCNUM	National drug code links to red book
	PAY	Pay represents transaction amount
	NETPAY	Net pay represents transaction amount from health plan
	AWP	Average wholesale price
	PLANKEY	Plan key is used to estimate market size
	PLANTYP	Plan type describes health plan type
	AGE	Age of enrollee
	SEX	Sex of enrollee
	EMPLOYECLAS	Employment classification of enrollee
	METQTY	Metric quantity of prescription filled
MarketScan® Outpatient Service claims	ENROLID	**
	DX1	Primary diagnoses listed by outpatient provider, used to identify cancer type
	DX2	Secondary diagnoses listed by outpatient provider, used to identify cancer type
Red Book®	NDCNUM	**
	GENIND	Generic indicator indicates if the drug is branded, multi source generic, etc.
	GENERID	Generic ID indicates NDC's that are therapeutically equivalent
	PRODNME	Product name for branded product
	MANNME	Manufacturer name link to NDC

Published Literature	OS_3	Overall survival >3
	FDA_YEAR	Year of FDA for indication

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Wiske, C. P., Ogbechie, O. A., & Schulman, K. A. (2015). Options to promote competitive generics markets in the United States. Jama, 314(20), 2129-2130.

Zafar, S. Y. (2016). Financial toxicity of cancer care: it's time to intervene. Journal of the National Cancer Institute, 108(5), djv370.

JEROMIE M. BALLREICH CV

Born January 17, 1984

EDUCATION

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
PhD Health Economics, 2017.
Doctoral Thesis: Price Discrimination in the US Cancer Drug Market
Committee: Gerard Anderson (Advisor), Kevin Frick, Karen Davis, Caleb Alexander, Antonio Trujillo

Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
MHS Health Economics, 2012.
Concentration: Comparative Effectiveness Outcomes Research

Lafayette College, Easton, PA
BA Mathematics and Economics, 2010.

RESEARCH EXPERIENCE

Major Extremity Trauma Research Consortium, 2011-present.
Research Assistant
Project: Economic evaluations alongside clinical studies targeting care of traumatic injured populations.

- Assist with Economic Analyses for six clinical studies
- Co-developed models to augment operations of METRC including Projection Tool for anticipated workloads, enrollments, and cash flow
- Co-developed process for incorporation of primary economic data alongside clinical studies

Bloomberg School of Public Health, 2012-present
Research Assistant with various faculty
Project: Arnold Foundation Project for High Cost Drugs

- Conduct policy analysis on policies to reduce high drug costs
- Participate in survey development to assess perceptions on fair drug prices

Project: Economic evaluation of pediatric asthma interventions targeting inner-city youth

- Conduct cost-effectiveness analyses for the Pediatric Asthma Management Feedback Intervention and the Asthma Express Intervention

Project: Economic evaluation of pelvic inflammatory disease intervention targeting inner-city youth

- Conduct cost-effectiveness analyses for the TECH-N Intervention

Project: Detention center bed forecast for Maryland Juveniles

- Conduct a bed forecast for Maryland Juvenile detention centers under different policy scenarios

Project: Commonwealth Fund Project for High Cost, High Needs patients

- Conduct qualitative literature search to identify successful interventions that target high cost, high needs patients within the US
- Participate in interviews and synthesize information across successful projects to identify trends

Project: Economic Evaluation of Intelligent Retinal Cameras for Diabetic Retinopathy in the Australian Aboriginal population.

- Evaluate the technical performance and cost effectiveness for screening of diabetic retinopathy using IRCs.

T. Rowe Price Equity Research Externship, Spring 2016.

Student Externship

Project: Work in a team researching publicly traded equities with a healthcare focus

Lafayette College, 2010.

Research assistant

Project: Measuring PCE Inflation and Core Inflation

- Assist faculty with analysis of various inflation measures using statistical techniques

FELLOWSHIPS AND AWARDS

The June Culley Scholarship in Health Policy and Management Doctoral Award, 2016.

The Jayne Koskinas Ted Giovanis Foundation for Health and Policy Dissertation Support Grant, 2015.

NRSA-HSR&P Training Grant in the Department of Health Policy and Management at the Johns Hopkins School of Public Health, 2012-2015.

Excel Scholar, Lafayette College, 2010.

Trustee Scholar, Lafayette College, 2002-2004

PROFESSIONAL ACTIVITIES

International Society for Pharmacoeconomics and Outcomes Research

President of Johns Hopkins Student Chapter, 2016-present

Member of Oncology Special Interest Group

Medical Care
Reviewer, 2016-present

International Journal of Technology Assessment in Health Care
Reviewer, 2015-present

SKILLS AND TECHNIQUES

Economic Modeling including Discrete Event and Markov-Simulations; Cost-effectiveness Analysis; Statistical Analysis; STATA; SAS; R Programming Language; Literature Reviews; Health Policy Analysis

TEACHING EXPERIENCE

Teaching Assistant, Economic Evaluation I, II, and III, Johns Hopkins Bloomberg School of Public Health, 2012-present.

Teaching Assistant, Public Health Policy, Johns Hopkins Bloomberg School of Public Health, Summers 2014-2016.

Teaching Assistant, Health Economics I, Johns Hopkins Bloomberg School of Public Health, Spring 2013 and 2014.

Teaching Assistant, Introduction to Health Policy, Johns Hopkins Bloomberg School of Public Health, Spring 2014.

PUBLICATIONS

Davis, K., & **Ballreich, J.** (2014). Equitable access to care—how the United States ranks internationally. *New England Journal of Medicine*, 371(17), 1567-1570.

Kleweno, C. P., O'Toole, R. V., **Ballreich, J.**, & Pollak, A. N. (2015). Does Fracture Care Make Money for the Hospital? An Analysis of Hospital Revenues and Costs for Treatment of Common Fractures. *Journal of Orthopaedic Trauma*, 29(7), e219-e224.

Butz, A. M., Ogborn, J., Mudd, S., **Ballreich, J.**, Tsoukleris, M., Kub, J., ... & Bollinger, M. E. (2015). Factors associated with high short-acting β 2-agonist use in urban children with asthma. *Annals of Allergy, Asthma & Immunology*, 114(5), 385-392.

Anderson, G. F., **Ballreich, J.**, Bleich, S., Boyd, C., DuGoff, E., Leff, B., ... & Wolff, J. (2015). Attributes common to programs that successfully treat high-need, high-cost individuals. *The American Journal of Managed care*, 21(11), e597-e600.

Sherry, M., Wolff, J., **Ballreich, J.**, DuGoff, E., Davis, K., & Anderson, G.F. (2016). Bridging the Silos of Service Delivery for High-Need, High-Cost Individuals. *Population Health Management*, 19(6), 421-428.

WORKING PAPERS

Ballreich, J., Burnett, A., Ho, A., Arkapaw, L., Kleinert, A., & Frick, K. (2016). Economic evaluation of an Automated Retinal Image Analysis in Australian Aboriginal and Torres Strait Islander populations for detection of Diabetic Retinopathy. (Under Review-International Journal of Technology Assessment in Health Care)

Alexander, G.C., **Ballreich, J.**, Socal, M., Karmarkar, T., Trujillo, A., Green, J., Sharfstein, J., & Anderson, G.F. (2016). Reducing Prescription Drug Spending Costs: A Review Of Policy Options. (Under Review)

Ballreich, J., Alexander, G.C., Socal, M., Karmarkar, T., & Anderson, G.F. (2016). Reducing Prescription Drug Spending: A Framework to Evaluate Policy Options. (Under Review-Journal of Pharmaceutical Practice and Policy)

Ballreich, J., Bai, G., Hsu, M., Traver, A., & Anderson, G.F. (2016). Dual Approaches for Estimating Drug Development Costs. (In Preparation)

Ballreich, J., Butz, A., Bollinger, M., Tsoukleris, M., Ogborn, C., Kub, J., Bellin, M., & Frick, K. (2016). Cost Effectiveness of Pediatric Asthma Management Feedback Intervention in High Risk Inner City Children. (In Preparation)

Chapter on Health Policy and Ethics in Oxford Handbook of Public Health Ethics, contributor. (In preparation)

POSTERS AND PRESENTATIONS

"Dual Approaches for Estimating Drug Development Costs." Accepted as Poster Presentation at 2017 ISPOR Annual Meeting.

"Reducing Prescription Drug Spending Costs: A Review Of Policy Options." Accepted as Poster Presentation at 2017 ISPOR Annual Meeting.

"Economic evaluation of an Automated Retinal Image Analysis in Australian Aboriginal and Torres Strait Islander populations for detection of Diabetic Retinopathy." *Best Student Research Podium* at 2016 ISPOR Annual Meeting.

"Does Fracture Care Make Money for the Hospital? An Analysis of Revenue and Cost for Treatment of Common Fractures", *Best Poster* in the Trauma classification at the 2014 AAOS Annual Meeting.

"Factors Associated With Recurrent ED Visits In Minority Children With Persistent Asthma", Poster at American Thoracic Society Annual Meeting. May 2015.

"Projecting Enrollment Across Multiple Studies in a Clinical Trials Consortium: a Forecasting Tool" Professional poster presentation at the DIA 2015 51st Annual Meeting. June 2015.

"What does it mean to be high-needs: a Patient's Perspective" Presentation at National Academy of Medicines Workshop on Models of Care for High-need Patients Workshop. July 2015.

"Needs, Barriers, and Opportunities Associated with Using Health IT: a personal Perspective" Presentation at Accessibility and Usability in Health Information Technology (HIT): A Research and Action Conference to Empower People with Disabilities, Older Adults, and Caregivers. September 2015.

"Community Services from a Patient's Perspective" Presentation at Patient-Centered Primary Care Collaborative Annual Meeting. November 2015.